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ORIGINAL ARTICLES

ENDOCRINE HOMEOSTASIS IN CLINICAL PEDIATRICS

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SIX MONTHS or a year ago it might have been appropriate to introduce these remarks with comments on the fact that endocrinology encompasses much more than the diagnosis and therapy of such primary endocrinopathies as pituitary gigantism, thyrotoxicosis, sex precocity and the like. The remarkable current reports on the therapeutic actions of adrenal cortical hormones and of pituitary adrenocorticotropic hormone (ACTH) already have shown that there may be as much or more endocrinology in a patient with rheumatoid arthritis, ruptured appendix, pneumonia, status asthmaticus or thermal burn as in the pituitary dwarf or eunuch. In fact it appears safe to say that there is hardly an organ or structure in the body that is not influenced directly or indirectly by endocrine forces or a clinical condition that is not accompanied by functional or homeostatic alterations on the activity of some endocrine gland.

These homeostatic reactions constitute to a major extent, as Walter Cannon once put it, "the Wisdom of the Body." Most of the time they work so efficiently that we forget that they exist and are playing an important role in bodily defense and recovery reactions. This thought may be worthy of illustration by a few arbitrarily selected situations. In presenting these illustrations I wish to emphasize that they represent the cumulative researches of many investigators working in many laboratories over a considerable period of time.

Figure 1 presents observations on a child with psychogenic polydipsia who was subjected to water restriction. This restriction was accomplished by omitting all fluids except those contained in solid foods. It is seen that such a physiologically normal individual is able quite effectively to conserve body H_2O (weight) and to prevent hemoconcentration (elevation in blood hemoglobin) by increasing urine solute concentration (specific gravity). This increase in concentration is brought about by an increase in posterior

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pituitary antidiuretic hormone (ADH) production. ADH production is controlled by hypothalamic osmo-receptors which Verney and others have shown to be acutely sensitive to changes in blood osmotic pressure.

Figure 2, which presents data obtained on a patient with diabetes insipidus, shows how seriously failure of this homeostatic mechanism handicaps an individual. Irrespective of the needs of the organism for water conservation, urine water output is determined by the load of solutes (osmoles) presenting to the kidneys for excretion. Consequently, upon water restriction or deprivation, H_2O is apt to be drained from the body with

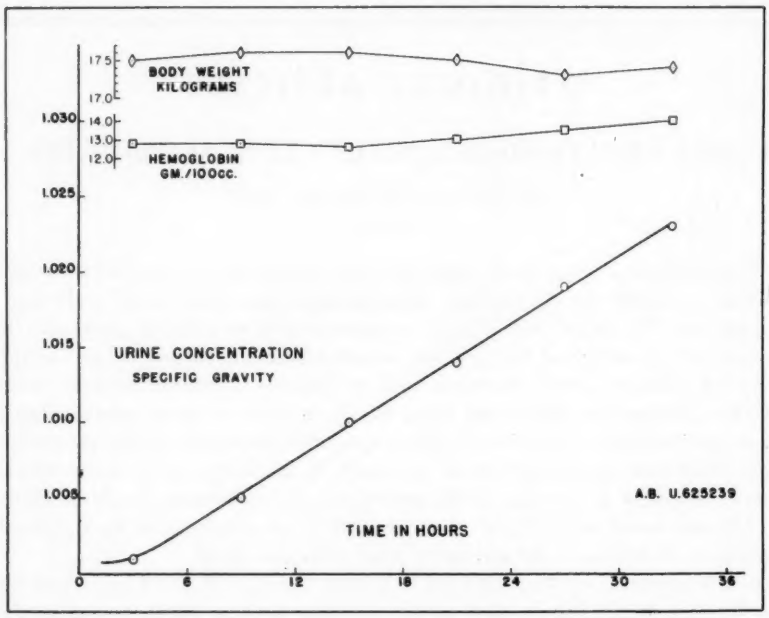

FIG. 1. Effect of restricting water intake to that contained in solid foods upon urine concentration, blood hemoglobin concentration and body weight of child with psychogenic polydipsia and polyuria. (From unpublished data of Crawford, J. D., and Talbot, N. B.[1])

resultant marked hemoconcentration and generalized dehydration (body weight loss). (See Fig. 3.)

Figure 4 presents some information concerning the opposite phenomenon of overhydration due to overloading of the ADH-renal water excretory mechanism with excessive amounts of H_2O. It is known that under conditions of zero ADH action and a sizable urinary osmolar load, maximum urine volumes are produced. In the human this urine volume is approximately equal to 15% of the glomerular filtration rate.* Stated in other words it is about 15,000 ml./m² (30 kg. child)/day. When the load of H_2O presenting to the kidneys for excretion exceeds this ceiling value, excess H_2O accumulates

* There is obligatory reabsorption of the other 85% of glomerular filtrate by renal tubules. In the adult glomerular filtrate volume is about 100 l./m²/day. In the newborn period it is about half that value.[2-4]

in the body and the blood becomes diluted. As this phenomenon becomes extended, circulatory collapse, renal failure, hematuria and death occur.

Such data remind us of the fact that we are constantly being served, in fact one might say saved, by this remarkable hypothalamic-posterior pituitary-renal mechanism. Provided this mechanism and the cardiovascular system are intact, one need not worry about administering any volume of isotonic, electrolyte-free H_2O which does not too closely approach the ceiling rate of 15 l./m²/day, or 10 ml./m²/minute. Recognition of this fact has aided us in the management of patients requiring parenteral fluid therapy. For example, Dr. James L. Gamble once pointed out that the factor which may determine more

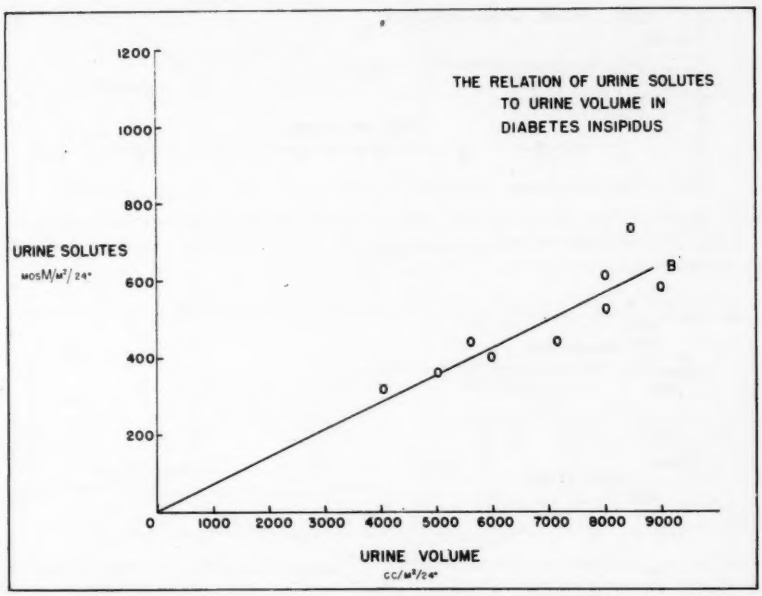

FIG. 2. Observations on relation between urine volume and urine solute (osmole) output of patient with diabetes insipidus. Note that relation between these 2 variables remains constant. (From unpublished data of Crawford, J. D., and Talbot, N. B.[1])

than any other the survival of infants suffering from severe chronic diarrhea is exhaustion of body caloric stores.[5] Simple calculations reveal that an adequate caloric intake can be provided by the intravenous administration of 5 or 10% dextrose in H_2O in amounts (for example, 6000 ml. of 5% dextrose/m²) which are comfortably within the limits just mentioned. The same thesis holds with respect to other substances which one may wish to administer but may hesitate to infuse in high concentration.

As a second illustration, one may turn to phosphorus homeostasis and the parathyroid glands. Figure 5 sets forth observations obtained in intact and parathyroidectomized rats. The abscissa indicates that groups of animals were fed rations varying in phosphate content* from nearly zero to the maximum quantity which can normally be eliminated

* Note that only a portion of phosphate intake is eliminated by way of urine; the remainder either is excreted in stools or incorporated in body tissue.

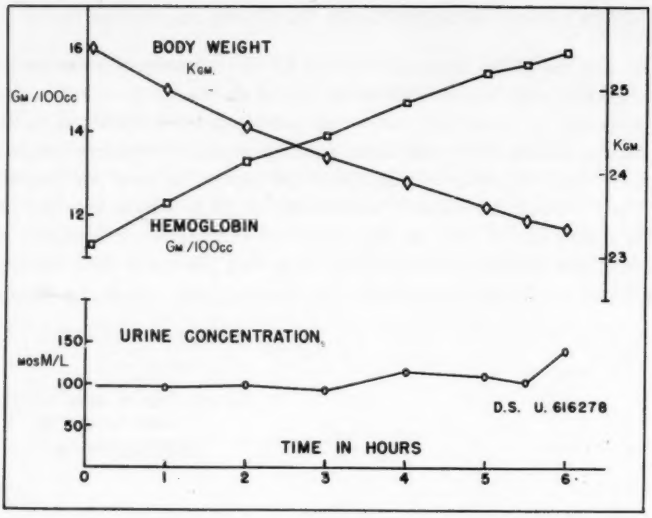

FIG. 3. Effect of water deprivation upon urine concentration, blood hemoglobin concentration and body weight of patient with diabetes insipidus. Patient of this experiment is same as that of Fig. 2. (From unpublished data of Crawford, J. D., and Talbot, N. B.[1])

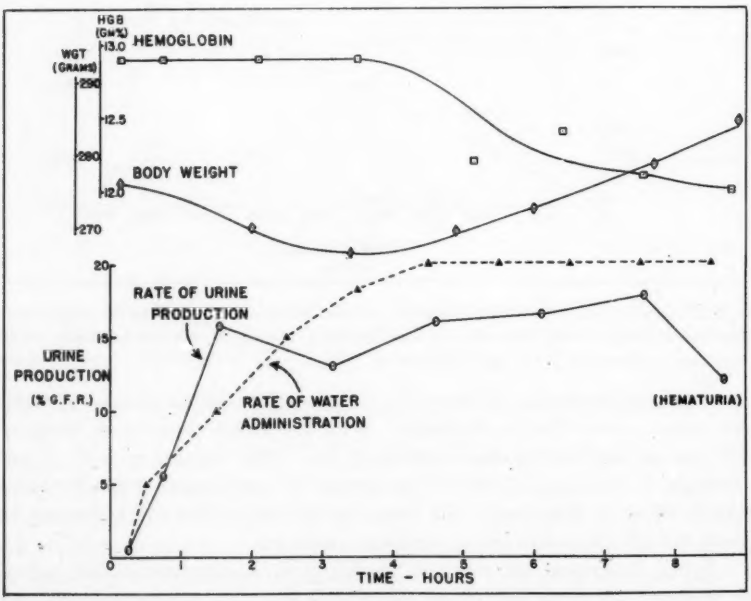

FIG. 4. Illustration of effect of increasing rate of water administration above physiologic limits upon rate of urine production, body weight and blood hemoglobin concentration of normal rats. Note that as rate of water administration is increased, there is compensatory increase in urine flow up to ceiling value equal to approximately 15% of assumed glomerular filtration rate of 50 l./m²/day. Incidentally, note also that increase in water intake initially resulted in overadjustment of urine water outgo. This resulted in transient period of body weight (water) loss which was unaccompanied by detectable changes in blood hemoglobin concentration. (From unpublished data of Crawford, J. D., and Talbot, N. B.[1])

with the aid of the parathyroid-renal mechanism without prompting significant pathologic disturbances in body fluid composition (i.e., serum phosphorus concentration). It is seen that the intact animals were able to take and excrete the various amounts of phosphate indicated without showing more than minor changes in serum phosphorus concentration. By contrast, it is evident that the parathyroidectomized animals developed marked hyperphosphatemia which culminated in tetany and death if their phosphorus intake was raised even slightly.

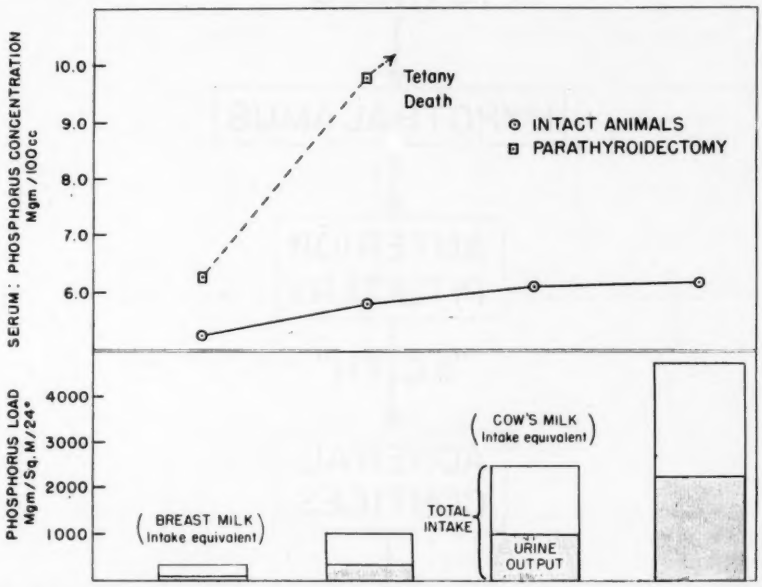

FIG. 5. Illustration of effects of varying phosphate intake upon urine phosphorus output and serum inorganic phosphorus concentration of normal, intact and of parathyroidectomized rats. Note that lower left-hand ordinate scale is expressed as mg./m²/24 hr. Because renal glomerular filtration rate in rats is approximately same as in newborn human infants (circa 50 l./m²/day), data shown for rats may be considered comparable to data obtained for young infants. Hence parenthetic indications of breast milk and cow's milk phosphorus intake equivalent. (From unpublished data of Crawford, J. D., Osborne, M. M., and Talbot, N. B.[6])

These phenomena find a counterpart in infant feeding. Note first that the infant fed human milk is receiving a phosphate intake comparable to the lowest recorded in figure 5. As recently shown by Drs. L. I. Gardner and A. M. Butler, such infants rarely show a pathologic elevation in serum phosphorus concentration.[7] By contrast, the infant fed a cow's milk formula is receiving a much higher phosphate intake. Infants over 3 to 4 weeks of age can assimilate and eliminate this higher phosphate intake without developing hyperphosphatemia. However, younger babies are apt, like the parathyroidectomized animals, to develop hyperphosphatemic, hypocalcemic tetany.

Studies have shown that this neonatal lack of ability to eliminate phosphate in accordance with need can be corrected experimentally by the administration of parathyroid extract.[6] In other words, tetany of the newborn infant is due to two factors: (a) tem-

porary failure of the parathyroid homeostatic mechanism and (b) transgression of the natural intent that human babies be breast fed.

As a third and final illustration, one aspect of the adrenal cortical "alarm reaction" to stress may be considered. Figure 6 shows how stress of any sort activates a chain of reactions which start in the hypothalamus, are mediated by the anterior pituitary and are culminated by an increase in adrenal cortical hormone production.[8] Figure 7 describes

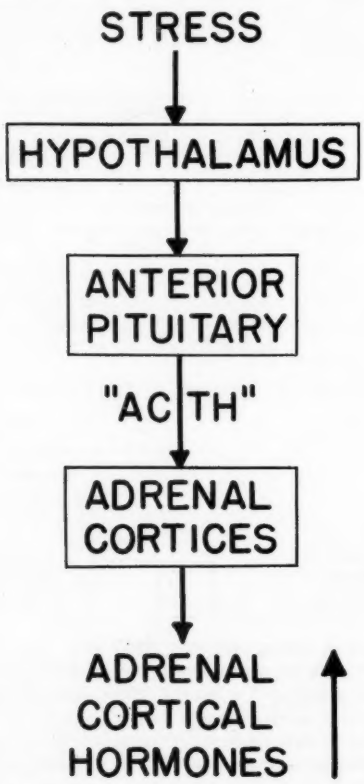

FIG. 6. Schematic presentation of mechanism by which stress may act to prompt increase in adrenal cortical hormone production.

diagrammatically one effect of these adrenal cortical hormones upon body metabolism. It is seen in the left-hand diagram that they act to limit Na and to facilitate potassium excretion by the kidneys.[9] These actions greatly increase the body's ability to support the vitally important extracellular fluid volume, if need be at the expense of some intracellular water depletion. As has been shown by Darrow and Yannet,[10] osmotic pressure relationships determine the distribution of water between extra- and intracellular compartments. Conservation of extracellular Na and elimination of intracellular K favor a shift of H_2O from the intracellular to the extracellular space.

In the right-hand diagram of figure 7 is shown the effect of giving isotonic saline under

such conditions of increased adrenal cortical activity. It is seen that the administered sodium salt is apt to exaggerate the homeostatic tendency to potassium excretion to a serious extent. The Na tends to enter the cells and to displace more K. There results a state of severe intracellular potassium deficiency. This is characterized clinically by somatic and cardiac muscle weakness, circulatory failure and death. As is being demonstrated with increasing frequency, these unfortunate phenomena can largely be prevented by administering solutions containing more physiologic mixtures of electrolytes, namely, solutions of nearly neutral ash and of approximately equal potassium and sodium content.

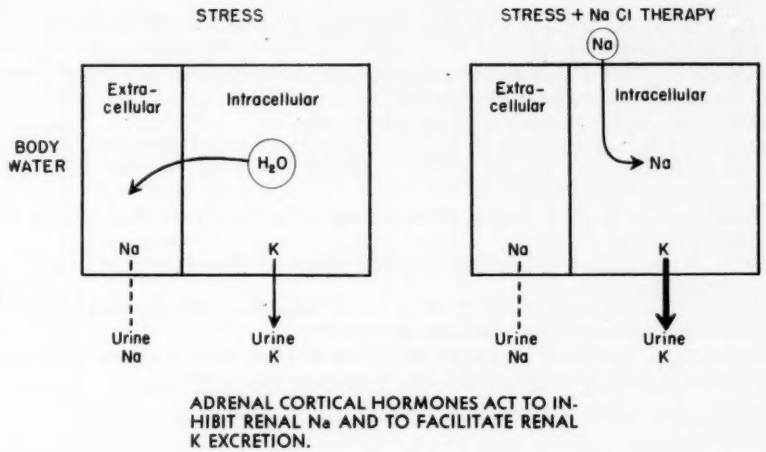

FIG. 7. Schematic diagrams showing how adrenal cortical hormones tend under conditions of stress to inhibit renal Na and to facilitate renal K excretion. As shown in left-hand diagram, this permits body to sustain extracellular fluid volume for time at expense of intracellular water if necessary. In right-hand diagram it is indicated that isotonic sodium chloride therapy may exaggerate tendency to intracellular potassium loss to pathologic degree.

In conclusion it may be said that the material just presented has illustrated only in part possible relations between endocrine phenomena and ordinary clinical problems. For example, no mention has been made of situations where homeostatic endocrine reactions appear, paradoxically, to be working against rather than for the best interests of the organism. Nor has much been said about natural and artificial factors which may modify the behavior of the glands of internal secretion and the concentrations of their respective hormones in the circulation. On the other hand, it is hoped that the material set forth adequately supports the thought that endocrinology can no longer be relegated to a small group of enthusiastic specialists. It must gradually become an intrinsic part of our regular medical practice.

ACKNOWLEDGMENT

In accepting this award I wish to express my appreciation to you who give it. I should also like to state my debt to my several associates in the Children's Medical Service at the Massachusetts General Hospital, especially Dr. John D. Crawford, Dr. Janet Mc-

Arthur, Dr. Edna Sobel, Dr. Concepción Uribe R., Miss Aniela Zygmuntowicz, Dr. Maurice Osborne, Dr. William Locke and Miss Elsie MacLachlan who have contributed in a very major way to any accomplishments which this award may recognize. Finally, it is a pleasure to acknowledge the generous support provided our research endeavors by Dr. Allan M. Butler.

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CONGENITAL ANOMALIES OF THE ESOPHAGUS

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AS THIS is the first general meeting of the Academy since the establishment of a surgical section, it would seem fitting to comment on our hopes for this venture. The last few decades have seen great advances in all fields of medicine. Among the most widely known, perhaps, are insulin, antibiotics, chemotherapy, water balance, vitamin and hormone therapy and other laboratory discoveries. I want, however, to call your attention to some of the advances which have been made in the field of pediatric surgery and to remind you that although these have been aided by laboratory achievements they would have been impossible without the cooperation of the pediatrician.

Please recall that roughly 30 years ago atresia of the bile ducts carried a mortality of 100%. Intestinal obstruction due to midgut volvulus had an equally high mortality. Congenital diaphragmatic hernia—other than those through the esophageal hiatus—had an estimated 90% mortality. The recovery of a patient with intestinal atresia was indeed a rare incident. The mortality from intussusception, and even from pyloric stenosis, was nearly 60%.

Today the mortality in these and other conditions has been reduced by from 25% to 75%, and in some conditions to nearly zero. This striking lowering of mortality has been brought about largely by men, both medical and surgical, who devote their energies to the care of infants and children. It seems, therefore, particularly opportune and appropriate that these pediatricians and pediatric surgeons should join together in a concerted effort to advance the care of this age group. I, for one, am sufficiently optimistic to believe that greater advances will be made in the decades to come if we all work together and with one goal in mind; namely, the improvement of the lot of the afflicted child. The establishment of a surgical section in this Academy certainly should help the pediatrician, the pediatric surgeon and last, but far from least, sick children.

So far as I know, no child with esophageal atresia born prior to November 1939 has survived. Before this date, many unsuccessful attempts to correct this anomaly had been made by various surgeons with different plans of attack. These attempts added to our knowledge of conditions which might be expected and paved the way for later successful results. Three fundamental conditions are essential for mastering this problem. First, the surgeon should have not only a delicate and refined technic but also a thorough knowledge of the variations of the anomalies which may be found and a plan for meeting them. He must also be accustomed to operating on small infants and use suitably sized instruments, needles and suture material. He must likewise be familiar with the pre- and postoperative care, including the fluid and feeding requirements of infants who undergo major surgical operations. In his team there should be an expert anesthetist for

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infants and an assistant with facility in isolating the small veins of infants for intravenous transfusion, medication or fluids, as indicated.

Second, early diagnosis and appreciation of the fact that infants in the first two or three days of life stand major surgical procedures far better than at the end of a week or later. This is particularly important in the cases of esophageal atresia, as infants with this condition usually develop aspiration pneumonia soon after birth which worsens the prognosis daily. The surgeon is at the mercy of the obstetrician, pediatrician or the general

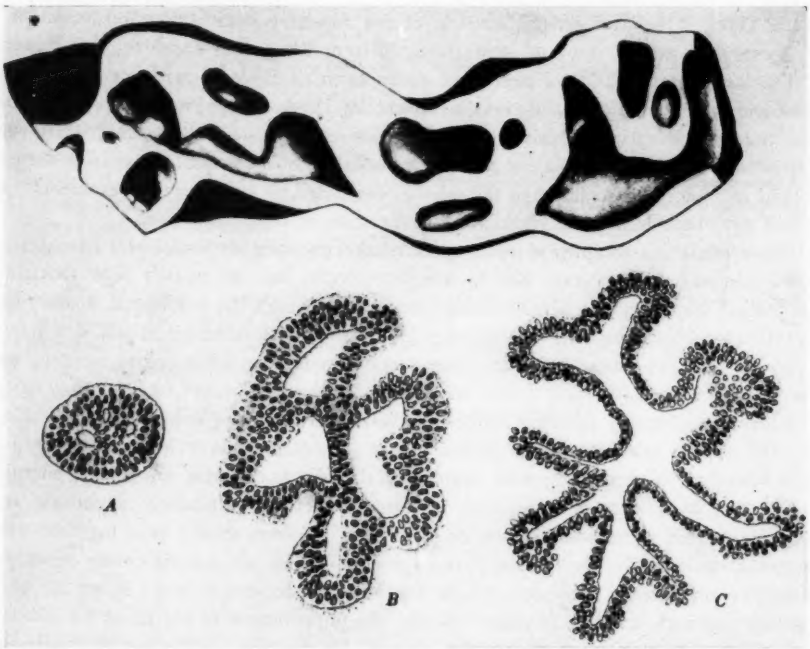


FIG. 1. (After Kiebal and Mall) Longitudinal section showing development of vacuoles in lumen. A. Transverse section showing lumen obliterated by epithelial concrescence. B. Development of vacuoles. C. Coalescence of vacuoles with lumen re-established.

practitioner for this early diagnosis and if they fail him a high mortality will result, no matter how good his operative technic may be.

Third, some knowledge of embryology is helpful in understanding the variations of esophageal atresia and tracheo-esophageal fistula and as stricture and duplications of the esophagus are really only variations of the same arrest in development these anomalies will also be mentioned.

Embryology: Between the 3rd and 12th week of fetal life great changes take place in the embryo and with amazing rapidity. (It is of practical clinical importance to remember this period of development as mothers are very prone to blame themselves for some incident near term for the malformation of their infant. It is gratifying to the mothers to be assured that such incidents could have nothing to do with the condition.)

The trachea and esophagus start as one tube and in the process of development become separated or pinched apart by the ingrowth of muscle and connective tissue. An arrest of this process or an incomplete separation leaves the two tubes connected with the resultant tracheo-esophageal fistula. This pinching off process may take place transversely as well as sagittally, causing the esophagus to end as a blind pouch or a stricture in case the pinching off is incomplete. Also, it is to be remembered that at this same time the lumen of the esophagus becomes obliterated by epithelial concrescence, resulting in

FIG. 2. A. Lumen obliterated by epithelial concrescence. B. Development of duplication with partition of mucous membrane and muscle layers. C. With partition of mucous membrane only.

an almost solid cord in place of a tube. As the esophagus lengthens the cord becomes vacuolated, the vacuoles coalesce and the lumen is re-established (Fig. 1). A failure of these vacuoles to coalesce sagittally could result in an atresia of the esophagus by a velum or, if this velum is perforated by a small hole, in stenosis or stricture. Failure of the vacuoles to coalesce transversely will result in a duplication and according to how much this development is combined with the pinching off process will depend what tissue lies between the duplication and the esophagus. There may be nothing but mucous membrane between the two or there may be also muscle and connective tissue, or in some instances they may be completely separated with a space between (Fig. 2).

Symptoms and Signs: The newborn infant who shows an excess of saliva in the mouth, with or without cyanosis, demands a very careful physical examination, bearing in mind the possibility of esophageal atresia. The chest examination may give signs of atelectasis, rales or pneumonia, most commonly in the right upper lobe. The abdomen may become distended and tympanitic after a few hours if the lower segment of the esophagus has a fistulous connection with the trachea. On the other hand, if there is no connection with the trachea one will find a scaphoid and nontympanitic abdomen. When the infant regurgitates almost immediately the first fluid given, one's suspicions should be increased and a soft rubber catheter (No. 8F or No. 10F) should be introduced into the esophagus. If this meets obstruction 10 or 12 cm. from the lips, the diagnosis is confirmed.

The only conditions which could be confused with esophageal atresia are esophageal stricture and congenital diaphragmatic hernia. In neither of these is the vomiting so

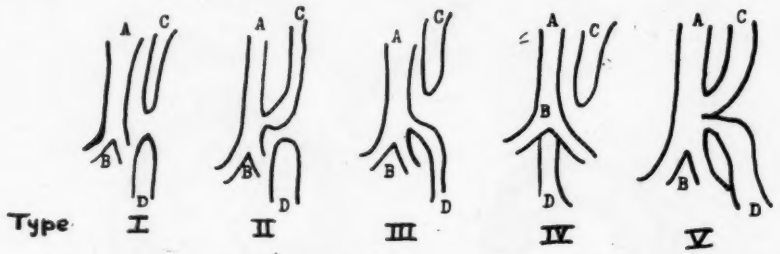


FIG. 3. Types of esophageal anomalies. (A) Trachea; (B) Bifurcation; (C) Upper segment of esophagus; (D) Lower segment of esophagus.

complete and with the help of the roentgenogram no difficulties should occur in differentiation. The vascular anomalies seldom or never have vomiting as the major symptom so soon after birth.

The next step is to determine the type of esophageal obstruction and the presence or absence of a tracheal fistula. These anomalies may be roughly divided into five types (Fig. 3). About 1 cc. of lipiodol is introduced through the catheter. If there is a fistula between the upper segment of the esophagus and the trachea, this can be demonstrated by the roentgenogram. At the same time the roentgenogram will show whether there is air in the stomach or not, which of course demonstrates whether or not there is a fistulous tract between the lower segment of the esophagus and the trachea. Caution should be taken not to use too much lipiodol as it will fill the bronchi, either through a fistula or by regurgitation and aspiration, which confuses the picture. Under no circumstances should barium be used as it will get into the lungs and increase the already existent pneumonia (Figs. 4, 5 and 6).

The diagnosis of esophageal atresia is not difficult to make and certainly should be made prior to the third day of life; yet in our experience such promptness is unusual and it is not uncommon for the pediatrician or general practitioner to delay a few days even after he has made the diagnosis. Such delay decreases very appreciably the chance of a successful outcome.

The diagnosis of tracheo-esophageal fistula without atresia is not so easy and may be difficult to confirm by either roentgenogram or esophagoscopy. I recall one patient that had respiratory difficulty after feeding, in whom I suspected the presence of a fistula. I

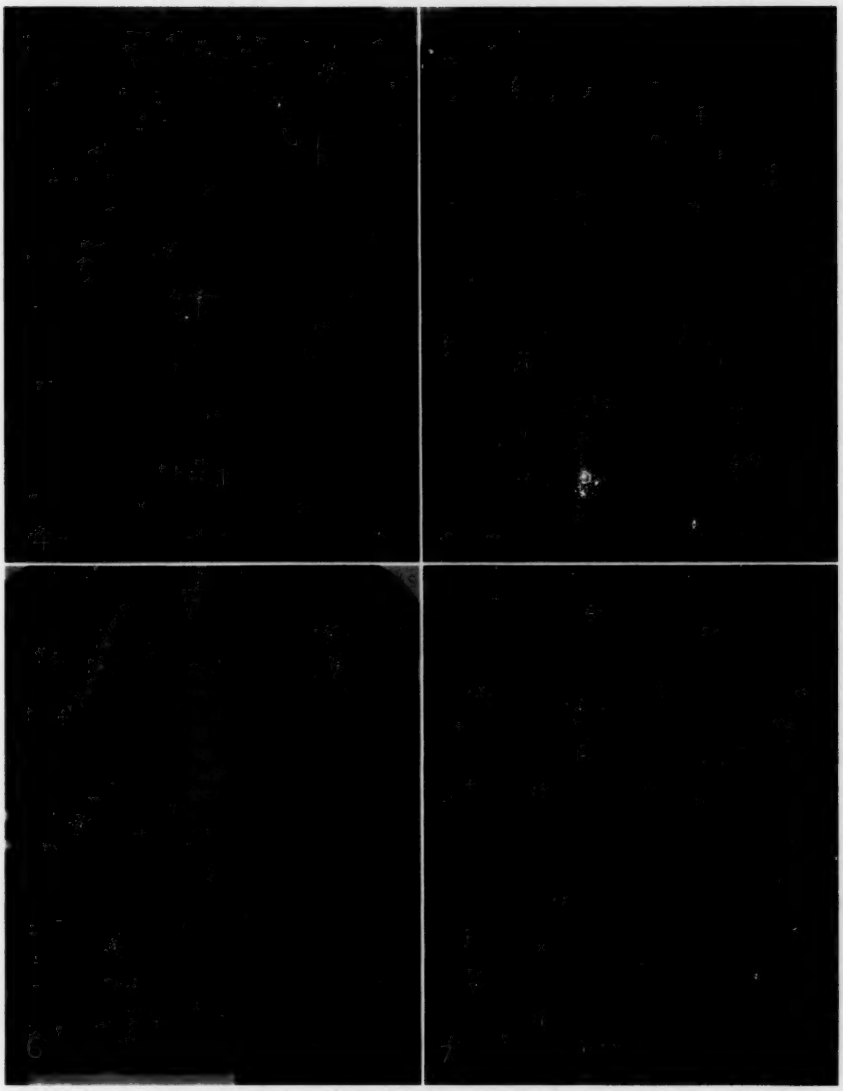


FIG. 4. Type 1 esophageal atresia. Note blind pouch containing lipiodol and absence of air in stomach.
FIG. 5. Type 3. Note blind pouch and stomach and intestine containing air.
FIG. 6. Atresia of esophagus, Type 3, and atresia of duodenum. Recovery after closing tracheal fistula performing duodenojejunostomy and later multiple stage procedure for reconstruction of esophagus.
FIG. 7. Tracheo-esophageal fistula.

refrained from operating because a fistula could not be demonstrated by either roentgenogram or esophagoscopy. That was a mistake as postmortem showed a small fistula that could have been remedied moderately easily. However, some fistulae may be demonstrated as shown in Fig. 7.

Stricture: The urgency of making the diagnosis of congenital esophageal stricture is not so great, as even a small opening will take care of the constant flow of saliva and some of the feeding for a week or 10 days. The occurrence of aspiration pneumonia though frequent is not uniform. Regurgitation immediately after feeding is the cardinal symptom and of course becomes more pronounced as the amount of the feeding is increased. The

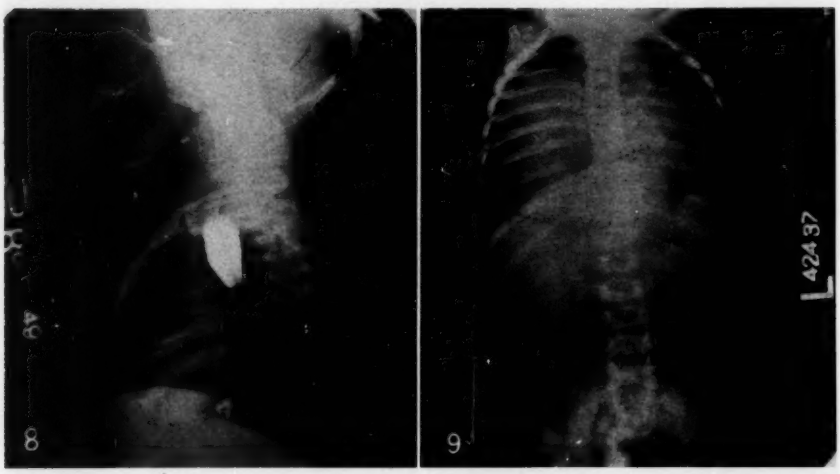


FIG. 8. Lateral view of esophageal stricture. Note trickle of lipiodol below stricture.
FIG. 9. Note smooth outline and uniform density of duplication occupying large portion of right chest and marked cardiac displacement to left.

roentgenogram of the esophagus containing lipiodol readily confirms the diagnosis (Fig. 8). These strictures are easily confused with a narrowing of the esophagus from spasm due to other causes than the arrest in embryologic development previously described.

Duplications are far more difficult to diagnose than the other anomalies of the esophagus. The symptoms are very variable and may not appear for several weeks, or even months, until the size of the cyst has gradually increased by the secretion of its mucous lining. Then the symptoms may be due to pressure causing respiratory difficulty, hemoptysis, recurrent attacks of respiratory infection or poor development. Occasionally, the cyst may be discovered accidentally in the course of examination in a child who has presented no symptoms referable to the duplication. The physical signs also may be very variable and may be masked by intercurrent pulmonary infection. However, on physical examination of the chest one may find in the back the classical signs of fluid, associated with a displaced heart. The roentgenogram may demonstrate a spherical mass of uniform density with a characteristically smooth outline. The roentgenogram may also show that this mass is retropleural and of course will demonstrate cardiac displacement if existent (Fig. 9).

Esophageal Stricture: There is a variance of opinion as to the best method of relieving congenital esophageal stricture. In selecting the form of treatment one should consider

the lesion and recall that it offers a very different problem from the lye stricture seen in older children.

The four plans that have been recommended are:

First: Dilatation through the esophagoscope. This method is dangerous except in the most expert hands and even then not as effective as other methods.

Second: Dilatation with a bougie and string guide. This has the disadvantage of the difficulty of getting the string down without a gastrostomy and also is not without danger on account of the stiffness of the dilators.

Third: Excision of the stricture with end-to-end anastomosis. This is a formidable operation to be resorted to only with special indications.

Fourth: Retrograde bouginage with the sausage-shaped, pliable rubber bougies introduced through a gastrostomy. This type of treatment has several advantages. The infant may be put and kept in good health by gastrostomy feedings. The bougies are pulled—not pushed; are flexible so that they can follow the curve of the esophagus, and large enough ones can be introduced to be effective. It is the safest and surest method in most cases.

Duplications: Duplications of the esophagus present difficulties not only of diagnosis but also of treatment. Complete excision is the operation of choice when feasible and when the duplication is completely separated from the esophagus. However, if you will recall the embryology, some cases are not completely separated from the esophagus but are closely fused with it, with no line of cleavage between the duplication and the esophagus. In such instances where there may be only two layers of mucous membrane between the duplication and the esophagus, it is almost impossible not to injure the esophagus with resultant leakage and fatal termination, or the development of postoperative stricture. This situation has been successfully overcome by excising as much of the duplication as can be done safely and marsupializing the rest to the skin in the back. The remainder of the mucous lining may then be destroyed by sclerosing and gauze packs.

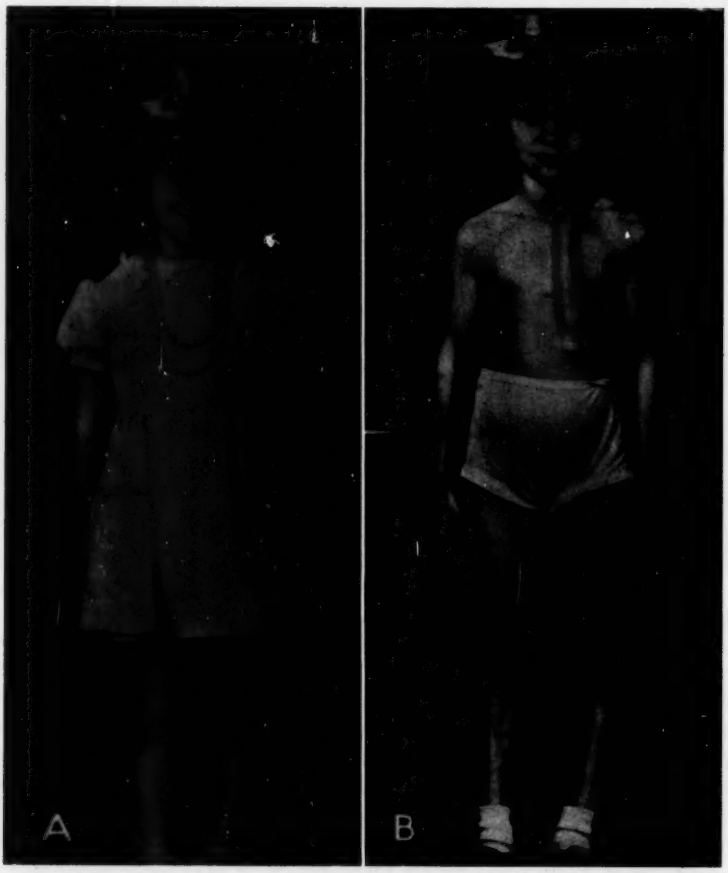
Of six duplications of the esophagus treated at The Children's Hospital, three could be completely excised and three were marsupialized. All recovered.

Preoperative Care of Esophageal Atresia: Chronologically the next important step after diagnosis of atresia is the preoperative care. As these patients usually have respiratory embarrassment from aspirated saliva and mucus, they should be placed in slight Trendelenburg position and constant suction of the pharynx applied. It is also desirable to place the infant in an oxygen tent. We also advocate a small transfusion but caution should be exercised with this or parenteral fluids to avoid amounts sufficient to cause pulmonary edema.

Anesthesia: Probably the most important factor of anesthesia is a good anesthetist with large experience in anesthetizing infants. Cyclopropane, or local anesthesia combined with cyclopropane, or at least combined with a closed respiratory system with oxygen available, have been the commonest agents used by us. The use of intratracheal anesthesia theoretically should be most desirable but using this method has been associated with a higher mortality rate than when a simple, tight-fitting mask and closed system were used.

Operation: The first successful operations were performed in multiple stages. The first stage consisted of exposing the esophagus and trachea retropleurally through the right back and obliterating the tracheo-esophageal fistula. The next stage—a day or two later—consisted of bringing the upper segment of the esophagus to the skin over the left clavicle and also doing a gastrostomy. This prevented any further aspiration of saliva and mucus and also prevented regurgitation of gastric contents to the lung. It also allowed adequate

feeding. The next steps consisted of connecting the esophagus to the intestinal tract. This was done by bringing a loop of jejunum anterior to the thoracic cage and anastomosing it directly to the esophagus or with a connecting link of a skin tube. By this plan we have 16 surviving children, the oldest being now 10 years old, leading quite normal lives. However, this plan requires many operations, long hospitalization and has other obvious



FIGS. 10 A and B. Author's oldest living patient, now 10 yr. old. Recovery after multiple-stage procedure.

disadvantages. With increased experience the direct anastomosis of the two segments of the esophagus became feasible and has supplanted the earlier plan (Fig. 10 A and B).

For the direct anastomosis, this approach may be made in the same way retropleurally through the right back. The anastomosis has been done also transpleurally as well as through the left back. The right retropleural approach, however, has sufficient advantages to make it the accepted standard. The tracheo-esophageal fistula is next excised and the fistula in the trachea carefully closed. The two segments of the esophagus are now freed sufficiently to allow approximation with as little tension as possible. The anastomosis is

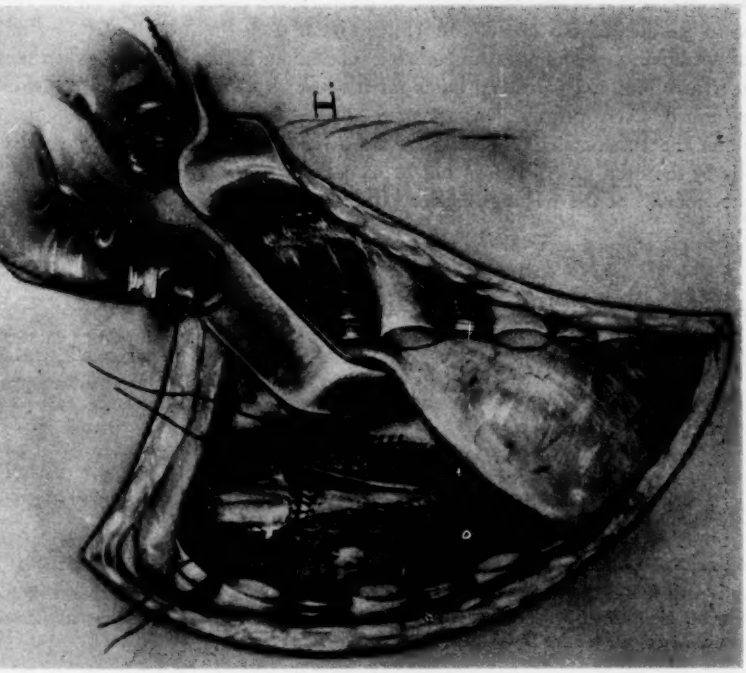


FIG. 12. Method of anastomosis of esophagus and closure of tracheal fistula.

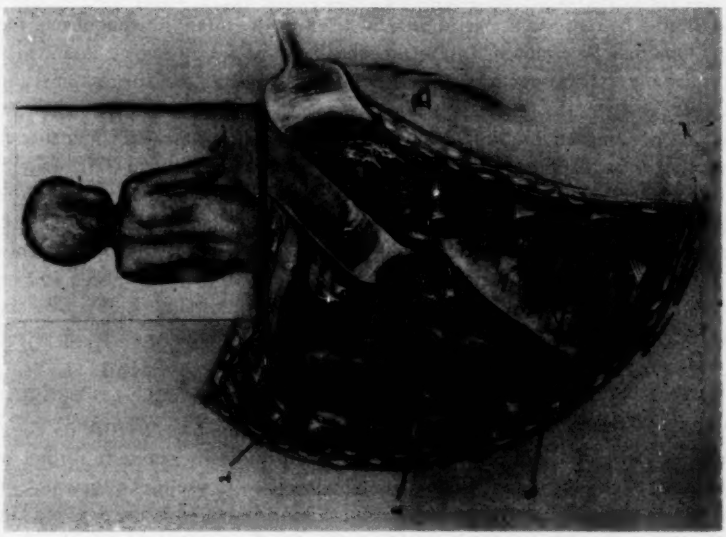


FIG. 11. A. Position of incision. B. Resection of 4 ribs: (1) vertebra; (2) azygos vein; (3) retracted pleura and lung.

done with two layers of interrupted silk stitches to avoid stricture and the incision in the thoracic cage and skin likewise closed to a small rubber tissue drain which has been inserted to the area of the anastomosis (Figs. 11 and 12).

Postoperative care is of great importance. The infant is placed in an oxygen tent and given transfusions and parenteral fluids for the first 48 hours or so. Then a gastrostomy is performed. Every precaution is taken to prevent retching or vomiting as this places strain on the anastomosis. The feedings are given in small amounts and very slowly, usually by the drop method which can be done so readily through the gastrostomy tube. As the amounts of the feedings are increased of course the amount of parenteral fluids

TABLE 1

PARTIAL LIST OF KNOWN RECOVERIES

Hospital*	Multiple Stage	Primary Anastomosis
	Living Patients	Living Patients
The Children's Hospital	16	63
University of Michigan Hospital	0	31
University of Minnesota Hospital	11	25
The Johns Hopkins Hospital	4	10
Total	31	129

* University of Michigan Hospital—Personal communication from Dr. Cameron Haight. University of Minnesota Hospital—Personal communication from Dr. N. Logan Leven. Johns Hopkins Hospital—Personal communication from Dr. William Scott.

can be decreased. At the end of a week or 10 days, feeding by mouth may be begun and as soon as this becomes sufficient in amount to meet the infant's requirements the gastrostomy tube may be removed. In the occasional case of a very rugged infant in whom an exceptionally satisfactory anastomosis has been possible the gastrostomy step can be omitted.

It has been estimated by Sir G. Gray Turner[1] that the congenital anomalies of the esophagus occur with approximately the same frequency as hare lip and cleft palate. If this estimate be accurate it suggests that we are less acute in our diagnostic ability than we should be. However, as an indication of improvement in diagnosis there have been approximately five times as many patients with this anomaly admitted to our Children's Hospital in the last decade as in the preceeding one. Since 1939 there have been 152 cases of esophageal atresia with 79 recoveries, which is a drop in mortality of 55% over the preexisting mortality of 100%. Table 1 made from personal communications gives a partial list of known recoveries.

COMMENT

The purpose of this paper has not been to present a complete treatise on congenital anomalies of the esophagus and many details are intentionally omitted; further reports can be found in the literature.[1-8] Our endeavor has been to use this subject as a vehicle to carry to you suggestions of some of the difficulties encountered in the field of children's surgery and some of the methods used to overcome them, and to urge the American Academy of Pediatrics to help raise the standard of children's surgery. It is our conviction that this Academy, which has proved itself to be so progressive, so industrious and so

efficient, can do much along this line if the members so desire. It is our hope that the Academy is broad-minded enough to feel that the surgical problems of early life are an important part of the general welfare of children and as such are of moment to it. We sense that the time is now ripe to make an effort.

Trees, in the shape of men devoting their whole time to advancing child surgery, have been planted in a few medical schools in the East, the Midwest and the far West. The Academy could do much in advocating that this become a more widespread policy. The establishment of departments of child surgery in the medical schools of the country would seem to be the next most logical step to take for the raising of the standard of surgery in this age group. Let us remember that team play is more important than individual effort and all work together for the general welfare of children on whom the future of our nation depends.

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Spanish Abstract

Anomalías Congénitas del Esófago

En este papel se consideran la atresia esofágica congénita, constricción esofágica, duplicidades esofágicas, fístula traqueoesofágica y sus variaciones. Se muestra el adelanto que se ha verificado en los últimos 10 años con 160 pacientes con atresia esofágica que han sobrevivido. Se discuten los métodos usados que han afectado este adelanto y se hacen sugerencias para el perfeccionamiento de la cirugía de niños en general en el siguiente comentario.

El objeto de este papel no ha sido el de presentar un tratado completo sobre anomalías congénitas del esófago y muchos detalles han sido omitidos intencionalmente. Hemos tratado de usar este sujeto como un vehículo para traerles a ustedes sugerencias de algunas de las dificultades que se han encontrado en el campo de la cirugía de los niños y algunos de los métodos usados para subsanarlas y pedir a la Academia Americana de Pediatría que ayude a levantar las condiciones de cirugía de los niños.

Es nuestra convicción que esta Academia, la que ha dado muestra de ser tan progresiva, tan industriosa y tan eficiente puede hacer mucho en este sentido, si así lo desea. Es nuestra esperanza que la Academia es suficientemente liberal para ver que los problemas quirúrgicos de la vida temprana son una parte importante del bienestar general de los niños y así es como le atañan actualmente. Creemos que el tiempo ha llegado cuando debemos hacer un esfuerzo.

En unas cuantas escuelas en el Este, Oeste central y el Oeste se han plantado árboles, en la forma de hombres que dedican todo su tiempo al adelanto de la cirugía del niño. La Academia puede hacer mucho para ver que esto se vuelva una política de gran propagación. El establecimiento de departamentos de cirugía infantil en las escuelas médicas del país serían el siguiente paso lógico a dar para levantar la norma de cirugía en este grupo de edad.

Recordemos que la solidaridad es más importante que el esfuerzo individual y todos trabajamos juntos para el bienestar general de los niños en quienes depende el futuro de nuestra nación.

Morgenster

ANGIOCARDIOGRAPHY IN INFANTS AND CHILDREN

New Technic

By JOHN D. KEITH, M.D., AND JOHN D. MUNN, M.D.
Toronto

WHEN a baby with congenital heart disease is born, the parents want to know immediately whether he is operable. This is especially true of the cyanotic group since the introduction of the Blalock-Taussig operation,[1] but it will be increasingly true for the noncyanotic group when the surgeons have perfected procedures for correction of the ventricular and auricular septal defects.

The importance of an accurate diagnosis is emphasized when it is pointed out that less than one half of the cyanotic group of the newborn period are amenable to surgery. Ordinary methods of examination frequently leave many diagnoses unsolved in early life. Cardiac catheterization is especially valuable for older children, but is difficult or impractical in infants. For this reason, the present authors have turned to angiocardiography to visualize the great vessels and heart chambers in this group. Acknowledgment is made to Castellanos,[2] Robb and Steinberg,[3] Sussman[4] and Neuhauser[5] for their many contributions on the use of this procedure in congenital heart disease. These investigators used technics which permit taking single roentgenographs or multiple roentgenographs up to one per second. Such serial roentgenographs following a diodrast injection may give considerable information, but in many cases one is limited by not knowing what was happening to the dye immediately before or after each roentgenograph was taken. For this reason and because Barclay et al.[6] found rapid serial roentgenographs useful in studying the fetal circulation in lambs, it was decided that a unit was needed that would take at least four roentgenographs a second.*

DESCRIPTION OF APPARATUS

The apparatus consists of a metal box (with a plywood top) which is 34″ long, 18½″ wide and 7½″ deep. On the plywood top there is outlined an area 9″ x 7″ to correspond to the film situated beneath. Over this area the chest of the infant is placed, usually in the LAO position. In the metal box there is a 12 volt d.c. geared-head motor. The motor turns at a speed of 8000 rpm. and is geared down to 200 rpm. The power source is stepped down from 110 v. to 12 v. and rectified to direct current by a selenium rectifier.

The motor also drives a drum-type switch or contactor operating a motor driven synchronous timer graduated in 0.05 sec. for timing the exposures. A tap switch connected to the power supply varies the voltage in order to control the speed of the motor.

The motor is connected to the film magazine or camera by means of an indexed spring-loaded cou-

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* Such a unit was constructed for the authors by Mr. William Burke of the Burke Electric and X-ray Company of Toronto.

pling in order that the magazine may be removed and placed again in the machine and still stay in synchronization with the contactor.

The film magazine is a Fairchild aerial camera magazine taking film 9″ wide and approximately 144″ long (exposed into frames 7″ x 9″). The drive shaft turns constantly driving a series of ratchets and cams that allow the film to travel 7″ and stop in 1 revolution of the drive shaft. The technical roentgenographic factors are usually as follows: KVA. 80, MA 200, target tube distance 30″, time 0.1 sec. or less. With these factors it is possible to take 4 frames/sec. It has been calculated by means of Victoreen ionization chamber that from the factors just mentioned the patient receives 7-10 r/35 consecutive exposures (in air).

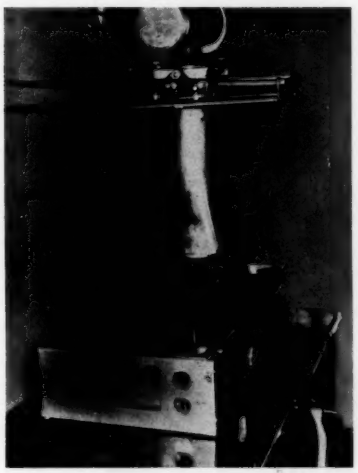


FIG. 1. Angiocardiographic apparatus consisting of rotating anode tube suspended over area covering rapidly moving film. Size of latter is indicated by marked rectangle. Conical shield is attached to tube and extends down to patient to prevent radiation to operator. Radiation is further controlled by small lead apron attached to cone on side of operator's hands.

For protection from the primary beam, a long metal cone extending from the tube to the patient is used and, in addition, lead rubber is draped around the end of the cone to protect the hands of the injector. The injector and nurse wear lead aprons (Fig. 1.).

The radiopaque dye used is diodrast® and concentrations ranging from 35 to 70% are used. The dye is injected as rapidly as possible into the femoral vein by means of an ordinary syringe with a #16 gauge needle, the vein having been prepared previously. Injection takes approximately 1 sec. Any longer than this allows the dye to become diluted. Infants are tested for sensitivity to the dye by injection of 0.5 cc. of 35% solution intravenously ½ hr. before procedure takes place.

The amount of dye used varies from 4 to 20 cc. depending upon size of the infant or child. The authors have used 5 cc./4.5 kg. body weight of a 70% solution of diodrast® when injecting babies. Older children have received less in proportion to body weight.

An example of the results with this technic is shown in figure 2. It is part of a roll of 20 roentgenograms (RGs) taken in the study of a normal heart. Each segment is 0.25 sec. from the next one. One can see the dye entering the heart, filling the R auricle, R ventricle and then the pulmonary artery.

RESULTS

There are no accurate figures available of the prevalence of the various types of congenital cardiac anomalies. Possibly Abbott's[7] summary on 1000 postmortem cases gives the best material. These have been reviewed and the 8 most common defects that produce cyanosis were determined and set down in the following table:

Pulmonary stenosis or atresia	122 cases
Transposition of great vessels	53 "
Dextrocardia	27 "
Complete defects of ventricular septum	22 "
Tricuspid atresia	16 "

Coarctation of the aorta	14 cases
Persistent truncus arteriosus	13 "
Aortic stenosis or atresia	11 "

The frequency with which these anomalies were found in Abbott's series fits in very well with the clinical experience at the Children's Hospital.

Since an angiocardiogram (ACG) is usually of more value in cyanotic cases than in the noncyanotic, efforts were directed chiefly towards demonstrating various R → L shunts. Cases with a L → R shunt

FIG. 2. Infants 3 wk. old. First 5 segments of roll of 22 roentgenographic reproductions taken 0.25 sec. apart. In 1st, dye is about to enter heart; in 2nd, it has filled R auricle; in 3rd, R auricle and ventricle are filled and in 5th, pulmonary artery is clearly outlined.

have been studied, but have not yielded as much information as cyanotic ones. These will be referred to later. As is well recognized now, the most common single type of anomaly that produces cyanosis in congenital heart disease is the tetralogy of Fallot. The ACG of such a case is shown in figure 3a. This is taken of a 3 wk. old baby who had a mild degree of cyanosis from birth. A faint systolic murmur was heard up the L border of the sternum and a continuous murmur in the pulmonary area. The ACG shows clearly the aorta overriding the L ventricle chiefly, but taking blood from the R ventricle as well. There is a complete absence of filling of pulmonary artery, but the aorta is clearly outlined.

Figure 3b is another case of tetralogy of Fallot in a baby 4 mo. of age with moderate cyanosis. The overriding aorta filling from R ventricle can be seen here. At the same time the pulmonary artery is clearly visualized—its branches are small. Figure 3c is a 3rd case of tetralogy of Fallot in a 5 mo. old baby. Both aorta and pulmonary artery fill simultaneously here. The pulmonary artery branches are close to normal size in this instance suggesting that the pressure is not conspicuously low.

The 2nd most common type of anomaly recorded is tranposition of great vessels. This defect commonly causes a severe cyanosis in early life and these cases are often seen much earlier than most of the tetralogy cases. Furthermore, these children live only a short time as a rule and this gives an opportunity, in many instances, to study the postmortem findings along with the ACG. Figure 4a shows the postmortem specimen of a case of transposition of great vessels in an infant 2 mo. of age. The aorta can be seen clearly coming off the R ventricle and the pulmonary artery off the L. There was no opening between the ventricles but an interauricular septal defect was present. This baby died between 3 and 4 mo. of age. About 1 mo. before she died, an ACG had been done and is shown in

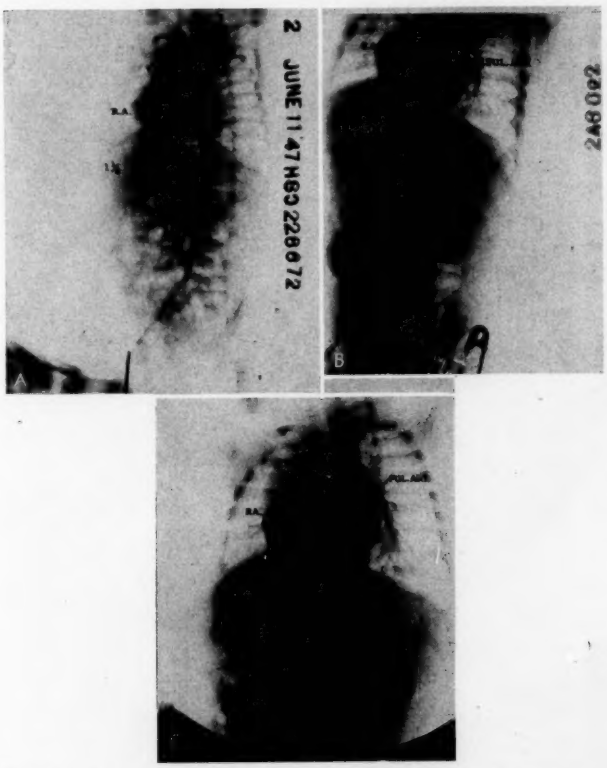


FIG. 3. Three cases of tetralogy of Fallot. a. Infant 3 wk. of age with moderate cyanosis; overriding aorta taking dye from R ventricle; no evidence of filling of pulmonary artery. b. Infant 4 mo. of age with moderate cyanosis; overriding aorta and pulmonary artery filling simultaneously from R ventricle; pulmonary artery branches smaller than normal. c. Infant 5 mo. of age with slight cyanosis; overriding aorta taking blood from R ventricle, pulmonary artery filling simultaneously, pulmonary artery branches almost normal size.

figure 4b. The R ventricle can be seen to have filled well with dye and the aorta filled immediately from it. Faint shadowing of dye appears in the L ventricle and L auricle and into the pulmonary artery; apparently it got there through the interauricular septal defect.

Figure 5 shows another case of transposition of great vessels in a 2 mo. old baby. In figure 5a R ventricle and 1st part of aorta are filled with contrast media and in figure 5b aorta is well outlined coming off the R ventricle, L auricle and L ventricle. Also shown is the increased density from diodrast® which has crossed through a patent foramen ovale. Figure 5c, taken 0.25 sec. later, shows pulmonary artery filling from L ventricle.

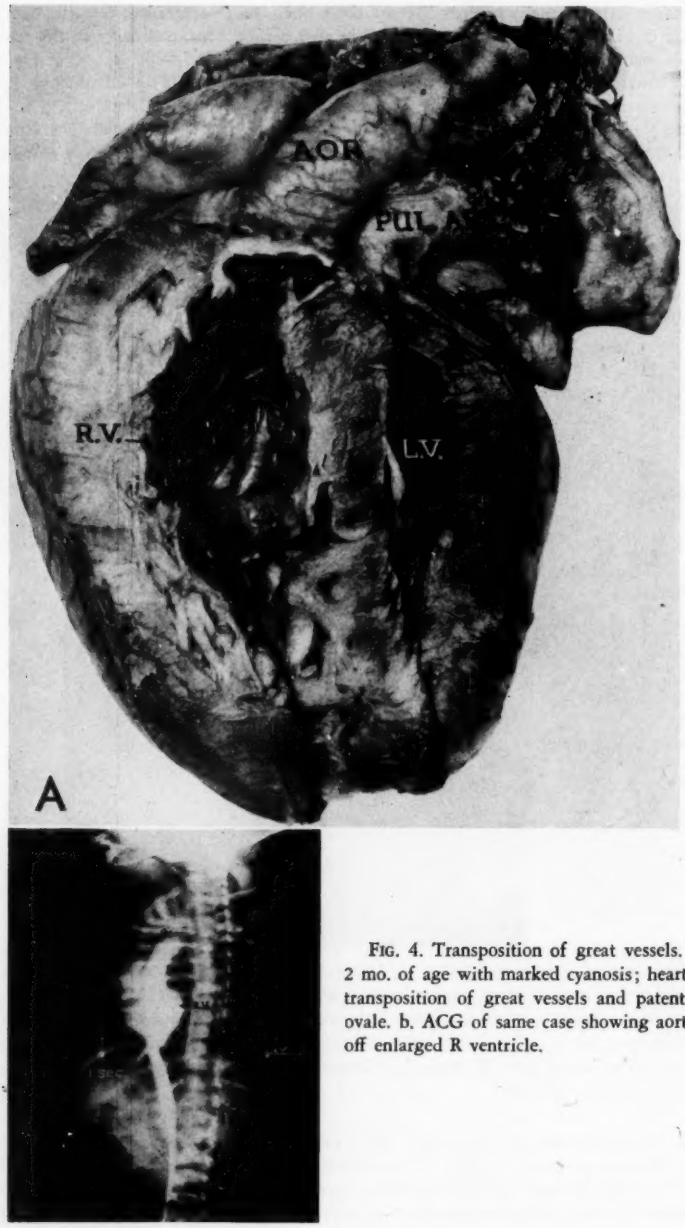


FIG. 4. Transposition of great vessels. a. Infant 2 mo. of age with marked cyanosis; heart showing transposition of great vessels and patent foramen ovale. b. ACG of same case showing aorta coming off enlarged R ventricle.

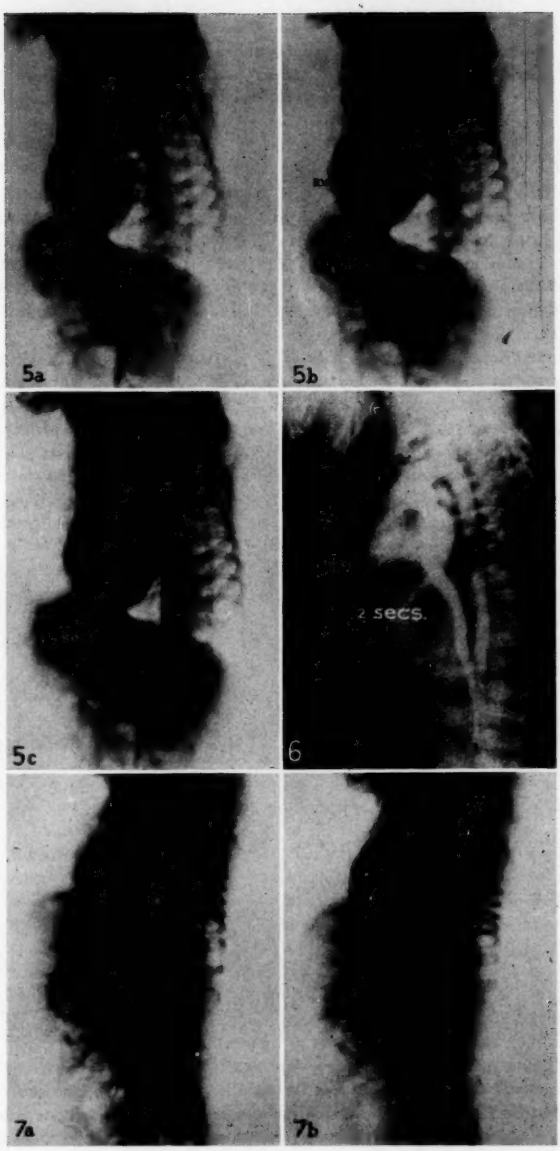


FIG. 5. Transposition of great vessels with patent foramen ovale. Infant aged 2 mo. with moderate cyanosis. a. One sec. after beginning of injection, aorta just beginning to fill from R ventricle. b. 0.25 sec. later; L auricle and ventricle show some filling. c. 0.25 sec. later; pulmonary artery outlined coming off L ventricle and slightly larger than aorta.

FIG. 6. Dextrocardia. Infant aged 4 mo. with cyanosis; hypoplastic pulmonary arteries, large interventricular septal defect, aorta coming off L ventricle.

FIG. 7. Large septal defect with transposition. Infant 1 mo. of age with marked cyanosis. a. One sec. after beginning of injection; contrast media bursting out into both R and L ventricles. b. 0.5 sec. later; dye coming off R ventricle into aorta and L ventricle becoming clearer.

The 3rd most common anomaly in the cyanotic group is dextrocardia. The cyanosis depends on associated defects, rather than on dextrocardia. These defects usually can be shown clearly by ACG.

An example of dextrocardia is that of a baby 4 mo. of age who had been cyanotic from birth. Fluoroscope showed heart to be entirely on R side of chest. An ACG taken in LAO position is shown in figure 6. The dye has entered R auricle, R ventricle and 2 hypoplastic pulmonary arteries and has also gone through a huge interventricular septal defect into L ventricle and thence to aorta.

Complete defects of ventricular septum are also common among cyanotic babies in the newborn period. They are the 4th on Abbott's list. The ACG of a 1 mo. old baby who had moderate cyanosis from birth is shown in figure 7a. Dye can be seen entering R ventricle and bursting over into L ventricle at the same time. In a subsequent ACG, L ventricle appeared relatively free of dye while the right continued to show dye indicating that the pressure was slightly higher in L ventricle than in R, but the force of injection of the dye was able to equalize these pressures and permit passage of dye from R ventricle over to L at that time.

The 5th commonest defect was that of tricuspid atresia or nonfunctioning R ventricle. These cases are relatively common at a children's hospital. The authors have had 5 within the past year. The diagnosis is usually easy with use of the ECG and the fluoroscope when the findings are typical, but it is important to know how readily the blood can get into the pulmonary circulation, the size of the pulmonary artery, and especially the size of the opening between the 2 auricles. The following case is that of a 3 mo. old baby who had L axis deviation in the ECG and when the dye was injected showed very clearly that it went across from R to L auricle and into L ventricle filling it well, and showing a dense concentration of dye (Fig. 8a). At the same time, the aorta filled and a small hypoplastic pulmonary artery could be seen in the ACG. This baby died a month or two later; a post-mortem specimen (Fig. 8b) is shown beside the ACG. There is a small interventricular septal defect into the vestigial R ventricle, normal pulmonary valves, and there is a good sized opening between the 2 auricles. The ACG (Fig. 8a) shows that concentration of dye in R auricle is considerably less than that in the L ventricle, even though dye is passing up the inferior vena cava at the time. This indicates that it passes readily from 1 auricle to the other and is not held up by the septum.

While the authors have not as yet encountered a case of coarctation of the aorta in the cardiographic studies on infants, the diagnosis has been suspected in several cases and dye injected up the brachial artery into the aorta. This can be done with relative ease and outlines the subclavian artery, and aortic arch and descending aorta as is shown in figure 9.

Figure 10 shows an example of what is believed to be a persistent truncus arteriosus. There is one large vessel coming off the centre of the heart and no evidence of any other large artery. This occurred in a 4 wk. old baby with marked cyanosis.

One occasionally runs into bizarre and unusual types of anomalies, such as the one shown in figure 11. This is the case of a 3 mo. old baby who had been cyanotic at birth and showed enlargement of the heart under fluoroscope. No significant murmur was heard and a definite diagnosis could not be made on clinical examination. However, when the ACG was taken it showed clearly that the aorta arose mainly from the R ventricle, whereas the pulmonary artery appeared to arise from both R and L ventricles, both vessels filling immediately the dye was injected. The pulmonary artery was a little larger than the aorta. This, it is believed, is an example of the new type of cardiac defect described recently by Dr. Helen Taussig and referred to now as the Taussig heart.

During the course of these studies, a number of interesting defects have appeared. Some have been merely of interest rather than importance, as the one shown in figure 12. Here the inferior vena cava has failed to join up with the vessel proceeding through the margin of the liver into the lower border of the R auricle. Instead it appears to have enlarged the azygos veins and entered the superior vena cava at the site of the greater azygos. Narrowing of the inferior vena cava in the lumbar region has been a common finding.

Another case, a 3 mo. old baby with cyanosis, revealed the defect shown in figure 13. In figure 13a the contrast medium is just entering the heart. In figure 13b it has filled the R auricle and furthermore has filled the radiating vessels. In figure 13c, 0.25 sec. later, these radiating vessels have emptied. On the strength of this evidence, it was suspected that a large interauricular defect was present allowing the dye to back up momentarily into the pulmonary veins. The dye appeared in the pulmonary artery branches (Fig. 13d) 1.5 sec. after the beginning of the injection. The baby died 1 wk. later and was found to have the large auricular septal defect shown in figure 13e. Complete diagnosis

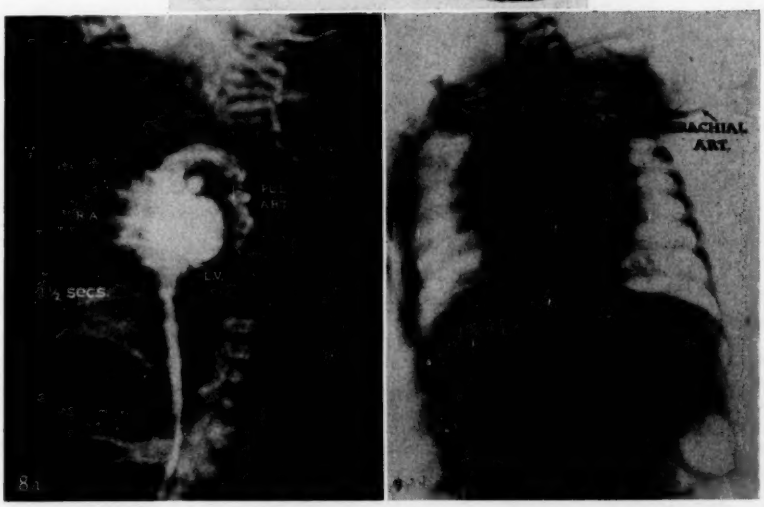


FIG. 8. Tricuspid atresia. Infant 3 mo. of age with moderate cyanosis. a. Diodrast® entering heart with no delay in R auricle, which is less dense than L ventricle. Film taken 1.5 sec. after beginning of injection; L ventricle fully filled and giving off aorta and dye entering small hypoplastic pulmonary artery. b. Postmortem findings of same case; complete tricuspid atresia, large interauricular septal defect, and tiny opening between enlarged L ventricle and vestigial R ventricle permitting blood to pass into hypoplastic pulmonary artery.

FIG. 9. Aortagram in baby aged 3 mo. Aorta is shown filling from L brachial artery. Case was suspected of being coarctation but no evidence of obstruction to flow of blood into aorta was found by ACG.

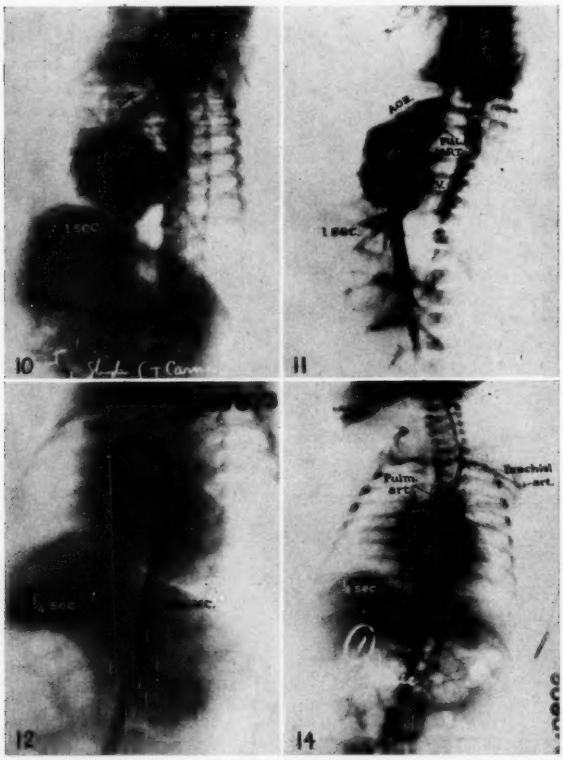


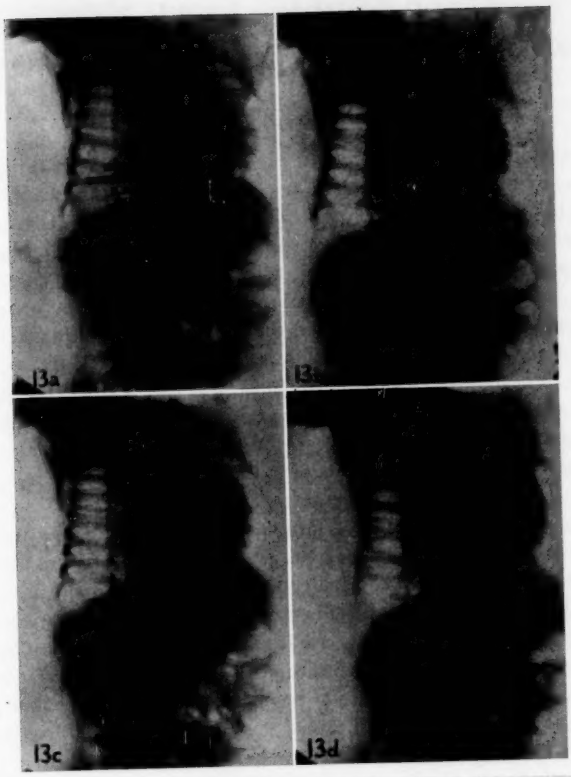
FIG. 10. Possible persistent truncus arteriosus. Infant 1 mo. old; 1 large vessel coming out of heart. Heart at 1.5 sec. completely and widely filled with diodrast®.

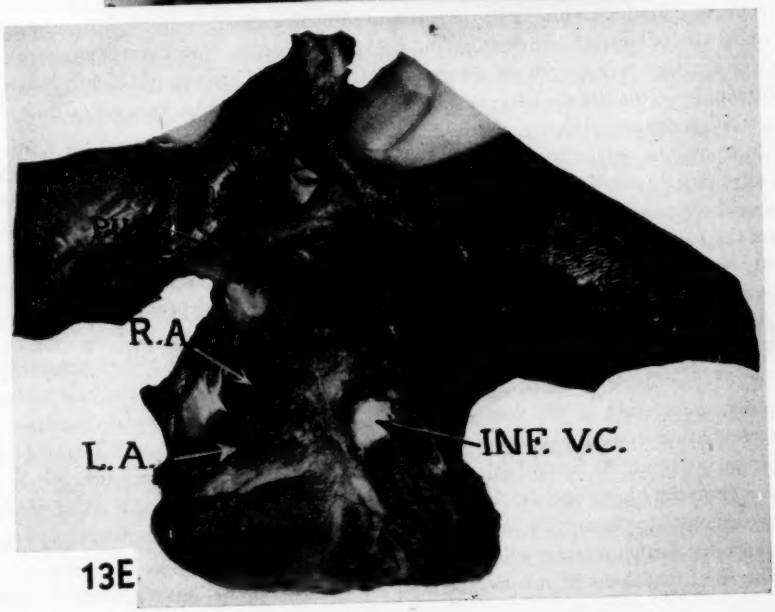
FIG. 11. Infant 3 mo. of age with slight to moderate cyanosis; both aorta and pulmonary artery filling immediately at 1.5 sec. from R ventricle. Pulmonary artery slightly larger than aorta and appears to take some blood from L as well as R ventricle. (Taussig heart.)

FIG. 12. Infant 4 mo. of age with cyanosis; at 0.25 sec., dye showed large uniform sized vessel proceeding up and arching over heart into superior vena cava at site of greater azygos vein (abnormal path of inferior vena cava).

FIG. 13. (See opposite page.) Interauricular septal defect; nonfunctioning R ventricle. a. Dye just entering R ventricle. b. 0.5 sec. later; dye entering R auricle and out into pulmonary veins. c. 0.25 sec. later; pulmonary veins have emptied again in that short interval. d. 1.5 sec. after beginning of injection, pulmonary arteries filling for 1st time. Diagnosis from these films was large interauricular septal defect. e. Diagnosis confirmed later at postmortem examination as shown in this figure. Hardly any division appeared between 2 auricles.

FIG. 14. Patent ductus arteriosus. In this 6 wk. old infant, contrast media has been injected up brachial artery back into aorta. Pulmonary artery is filling from aorta via patent ductus arteriosus.





13E

at autopsy was auricular septal defect, pulmonary stenosis, nonfunctioning R ventricle and rotation of the heart.

Comment

Since Castellanos began his studies with angiocardiography in 1937, this approach has frequently proved useful in investigation of congenital heart disease. When cyanosis is present, the radiopaque media will often reveal an outline of the aorta overriding the right ventricle. It may show an interventricular septal defect or an interauricular septal defect. In tetralogy of Fallot, the size and patency of the pulmonary artery can often be demonstrated. In newborn babies, congenital cardiac anomalies are encountered with considerable frequency. At such an early age the anomalies are usually difficult to name, especially when one realizes that there are over 100 different types. Angiocardiography is of some value in nearly every case studied; in some it may make a clearcut diagnosis, in others, it may simply add minor details to the case. In the past a great many angiocardiographic studies have been based on using a single roentgenogram taken 1 or 2 seconds after the beginning of injection of diodrast® intravenously. Using this technic the authors collected some information. Recently, however, it has been found that the technic of using rapid serial roentgenograms gives more information than a single one; for example, one may then go over a group of roentgenograms and select the best film or films to show the defects present. One cannot predict usually with certainty just when is the optimum time to take a single roentgenogram following a diodrast injection in cyanotic infants. It is probably between 1 and 2 seconds after the beginning of the injection of the dye into the blood stream but 0.25 second makes considerable change in the appearance and position of the dye so that having a large series of roentgenograms taken in a short space of time allows one to select the best 4 or 5 for special study. In the noncyanotic group, roentgenograms at intervals over 8 to 10 seconds may be desirable. Frequently it has only been possible to tell which path the blood is taking through a grossly abnormal heart by careful examination of several roentgenograms 0.25 second apart. Roentgenograms taken one second apart go a long way to answering many of the diagnostic problems, but would fail to pick up the defects such as shown in Case 13 which only revealed an anomaly in one roentgenogram in the entire series.

In a cyanotic infant with a shunt from the right ventricle into the aorta, the dye is rapidly cleared from the heart. In a normal infant it usually takes a matter of 6 to 8 seconds before the circulation through the heart is complete; in cyanotic infants the dye is cleared from the heart in 2 to 3 seconds except for small quantities returning from the lung. Recently we had occasion to do a single film after an angiocardiogram; after being used to viewing 20 serial films 0.25 second apart, we realized how dependent we had become on being able to review the whole cycle in detail.

Theoretically the more frequent the roentgenograms can be taken with this technic, the better. If they could be taken at moving picture speed of 16 frames a second or faster, opening and closing of the valves would be apparent. This has been demonstrated by Warren,[8] using moving pictures of the fluoroscopic image in animal studies, taking up to 40 frames/second. At present it is not known how much more information can be obtained from the higher speeds. A number of defects have been found that could not have been demonstrated except by increasing to four frames a second and one might readily presume that further increase will add to the detail available.

The chief usefulness of this technic is in the newborn period when a diagnosis is par-

ticularly difficult. The present investigators have examined 60 cases in this manner and have yet to find two alike. Even in cases of tetralogy of Fallot all show minor or major differences. In the tetralogy group one can outline the pulmonary artery in most cases, and it should be possible to outline it when an opening exists from the right ventricle into the pulmonary artery.

Experience with the noncyanotic infant has been more limited. Perhaps the most striking result of investigation in this group was to find that a patent ductus arteriosus could be demonstrated by injecting the contrast media up the brachial artery into the aorta. One or two of the series of roentgenograms in this type of case will then show filling of both the pulmonary artery and the descending aorta from the aortic arch. This is often an unexpected finding since there may be no murmur indicative of a patent ductus in early life. In the left anterior oblique position the ductus arteriosus connecting aorta and pulmonary artery can be visualized (Fig. 14).

A ventricular septal defect can be demonstrated frequently in the cyanotic group. In the noncyanotic the evidence is more indirect. Here again one is helped by the multiple serial roentgenograms, since the pressure of a high ventricular septal defect causes continual refilling of the pulmonary artery from the left ventricle, and one then finds contrast media in the pulmonary artery long after it would be expected to have cleared entirely.

A patent foramen ovale may be demonstrated by this technic by observing the first half dozen roentgenograms in the series. Here one can see the right auricle fill and then a faint shadow appear in the left auricle and left ventricle. A large interauricular defect may be shown by filling of the pulmonary veins in the first second after the beginning of injection, as was demonstrated in Case 13.

Much has been written[9] about the dangers of the rapid injection of diodrast® intravenously. Nearly every centre has had at least one fatality in angiocardiography. At the Hospital for Sick Children, there was one such death. This occurred in a 3 year old child who was cyanotic and at postmortem was found to have tetralogy of Fallot with pulmonary atresia. The blood supply to the lungs was through a small recurrent artery from the neck into the pulmonary artery. It was well recognized that diodrast® produces a slight drop in blood pressure, and in this case it may have been enough to seriously impair the already scant blood flow to the lungs. The infants injected have tolerated the dye quite well. The noncyanotic ones usually give a slight cough and show some degree of flushing of the skin. The cyanotic babies are less likely to cough but may become a shade more cyanosed in a few minutes. Infants tolerate the dye as well or better than older children. The authors' experience suggests that it is quite safe to investigate infants in the first week or two of life.

The greatest danger arises from a second injection of the contrast media within a half to an hour of the first one. It is known that fatalities have been produced in this manner. One child in this group collapsed temporarily when a second injection was given one half hour after the first. Following this latter case, it was decided not to give more than one injection of the contrast media on the same day. It appears from the literature[9] that we may expect fatalities to occur at long intervals even with the most careful technic. For this reason each case should be considered separately as to whether the procedure is warranted. The majority of the cases in this study have been in the first few weeks or months of life and are usually quite cyanotic. In such infants the diagnosis is usually difficult by clinical methods and the wealth of information obtained by this technic of rapid serial roentgenograms amply justifies the procedure.

SUMMARY

An apparatus is described which permits taking four roentgenograms/sec. Its use in angiocardiography is demonstrated by a series of cases with congenital cardiac anomalies. This method of investigation has proved most useful in studying the cyanotic group and in demonstrating shunts from right to left. A variety of different technics may, however, yield useful information in the noncyanotic group also. The procedures outlined are most valuable in the newborn period where congenital cardiac anomalies are so commonly encountered and where their differentiation is particularly difficult. The information collected in this manner has been, in many instances, a help to the surgeons in planning suitable surgery.

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SPANISH ABSTRACT

Angiocardiografía en Infantes y Niños; Nueva Técnica

Se describe un aparato el cual permite tomar cuatro roentgenogramas/sec. Su uso en la angiocardigrafía se demuestra por una serie de casos con anomalías cardíacas congénitas. Este método de investigación ha resultado de muchísima utilidad en el estudio del grupo cianótico y en la demostración de desviaciones de derecha a izquierda. Una variedad de diferentes técnicas pueden, sin embargo, producir información útil también en el grupo que no es cianótico. Los procedimientos descritos son de mucho valor en el período del recien-nacido cuando generalmente se encuentran anomalías cardíacas congénitas y cuando la diferenciación es particularmente difícil. La información coleccionada de esta manera ha sido, en muchos casos, una ayuda a los cirujanos al planear la cirugía adecuada.

67 College Street

RECOVERY FROM INFLUENZAL MENINGITIS WITHOUT INTRATHECAL THERAPY IN A FOUR DAY OLD INFANT

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Memphis

ALTHOUGH influenzal meningitis is a commonly recognized disease in infants under 2 years of age, it is extremely rare in the first days of life. Kagan and his associates[1] have recently emphasized the rarity of all types of meningitis in premature infants but had no cases due to H. influenzae type B in their own series. Fothergill and Wright[2] reported an incidence of 0.5% under 1 month of age in a review of 200 cases of influenzal meningitis. In 76 patients of their own, none was under 1 month of age. Yampolsky and Jones[3] recently reported a patient 1 day of age in a review of 22 cases of this disease. This patient recovered after receiving streptomycin both intramuscularly and intrathecally. The purpose of this report is to present a case of influenzal meningitis in a 4 day old infant who recovered without intrathecal medication.

CASE REPORT

R. D., a 4 day old Negro male, was admitted to the Childrens Hospital. The history revealed that the mother was gravida 1 and, with the exception of Grade I toxemia, had had a normal pregnancy and labor. The infant was delivered as a normal spontaneous breech and was given oxygen and artificial respiration for a short period. A tracheal catheter was inserted to remove any accumulated mucus. Following the delivery, the infant appeared normal, weighing 3.0 kg. Due to the crowded conditions of the maternity wards, he was discharged from the newborn nursery on the 2nd day of life. Later that day, the infant exhibited anorexia and a progressive increase in irritability. Fever became evident to the mother 24 hr. before readmission to the hospital.

Physical examination showed the patient to be well-developed and well-nourished, but mildly dehydrated. The temperature was 39.4° C., pulse rate 140/min., respiration rate 22/min. and the weight 2.8 kg. The infant was irritable and cried during the entire examination. Anterior fontanel was full and bulging slightly but not tense. There was no nuchal rigidity and the Brudzinski and Kernig signs were absent. Moro reflex and tendon reflexes were normal.

Admission laboratory findings were: Hgb. 12 gm./100 cc. blood, RBC 4.8 million/cmm. and WBC 11.9 thousand/cmm. Differential count showed neutrophilic metamyelocytes 14%, nonfilamented neutrophils 18%, filamented neutrophils 36%, lymphocytes 27%, large monocytes 4% and basophils 1%. A blood culture was obtained on admission which later revealed a growth of H. influenzae type B.

The infant was given subcutaneous fluids and placed on an evaporated milk formula. Slight improvement was noted within the 1st 20 hr., the temperature falling to 37.3° C. However, several hours later, the temperature began to rise, and re-examination while the infant was quiet again revealed a full and slightly bulging fontanel. A lumbar puncture was performed at this time and revealed a turbid fluid under increased pressure; the findings of this and subsequent punctures are recorded in table 1. In addition, the Gram stain of the cerebrospinal fluid revealed predominantly gram negative rods and occasional gram negative diplococci. Capsular swelling was demonstrated using H. influenzae type B specific antiserum. Initially, dihydrostreptomycin 150 mg. was given intramuscularly and followed by 50 mg. every 8 hr., intramuscularly. In addition, the patient was given aqueous

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TABLE 1

CEREBROSPINAL FLUID AND BLOOD FINDINGS

CEREBROSPINAL FLUID

Hospital Day	1st	3rd	5th	7th	9th	21st
Appearance	Cloudy	Slightly cloudy		Clear	Clear	Clear
WBC	3000	564		342	148	27
Differential						
Polys. %	95	82		40	44	4
Lymphs. %	5	18		60	56	96
Culture	H. influenzae type B.*	No growth		No growth	No growth	No growth
Protein mg./100 cc.	220	165		174	147	94
Sugar mg./100 cc.	12	35		48	44	56
Chloride mEq./l.	123				117	116
Streptomycin Level μg/cc.		20	10	5	5	
Penicillin Level u./cc.		0.25	1	2		

BLOOD

Culture	H. influenzae type B.	Negative	Negative		Negative	
Streptomycin Level μg./cc.		More than 80	20	20	10	
Penicillin Level u./cc.		More than 24	16	16		
Sulfadiazine Level mg./100 cc.		17.5	8.2		7.4	

* Sensitive to streptomycin in concentration of 6.5 μg./cc. and sulfadiazine 20 mg./100 cc.; not sensitive to penicillin concentration of at least 25 u./cc.

penicillin 1 million units as an initial dose intramuscularly, and 1 hundred thousand units every 3 hr., as well as sodium sulfadiazine 0.4 gm. immediately and 0.2 gm. every 6 hr. The sulfadiazine was given as a 5% solution in physiologic saline subcutaneously.

The cerebrospinal fluid culture, as well as the admission blood culture, was positive for H. influenzae type B. Sensitivity tests revealed that this organism was insensitive to penicillin up to concentrations of 25 u./cc., the upper limit of the test used. However, its growth was inhibited by a concentration of streptomycin 6.5 μg./cc. and sulfadiazine 20 mg.%. Reference to table 1 shows that adequate therapeutic blood and cerebrospinal fluid levels of streptomycin were obtained within the 1st 36 hr. The table shows further that these levels remain adequate for the 1st 5 days of therapy. The penicillin and sulfadiazine levels as well as sensitivities are also shown in the table.

After the institution of therapy, there was progressive clinical improvement. Temperature became normal within 48 hr. and remained so except for a rise to 38.1° C. 13 days after admission. This rise was attributed to an abscess of the buttocks. The anterior fontanel was soft and easily depressed 72 hr. after beginning treatment. The formula was retained at all times and there was a steady weight gain. Penicillin was discontinued after 13 days. In view of the lack of sensitivity of the organism, it might well have been discontinued earlier. Sulfadiazine was continued throughout the hospital course and 2 small blood transfusions were given as supportive therapy. The patient was discharged on the 25th hospital day.

One month after discharge, RGs of the skull showed no evidence of increased intracranial pressure. The infant had progressed well and the entire physical examination, including measurement of the head circumference, was normal.

EEG done before discharge showed phase reversals in the frontal and occipital areas. Four weeks after discharge, a tracing was interpreted as showing partial suppression of cortical activity in the frontal areas. However, another EEG done 6 wk. after discharge was normal.

Discussion

Many investigators[4-7] have advocated the intrathecal administration of antibiotics in the treatment of the meningitides. Other authors[8,9] have stated that this procedure is not only unnecessary but dangerous. Dowling and his associates[10] have recently demonstrated that large parenteral doses of penicillin can be used successfully in the treatment of certain cases of purulent meningitis without intrathecal medication. Alexander and Leidy[11] have proposed that only a single intrathecal injection of streptomycin be given in treating H. influenzae meningitis.

This case is of interest because it demonstrates a successful therapeutic result without intrathecal medication in an age group where meningitis of any type is especially serious. However, this report is not offered as a basis for recommendation on therapy of all cases of meningitis in infancy and childhood.

The cerebrospinal fluid level of streptomycin of 20 μg./cc. is higher than that obtained in older infants and children. The high level in this case may be accounted for in part by an increased permeability of the meninges during the early newborn period when compared to older infants. Also, the blood levels of streptomycin were high and perhaps reflect the relative immaturity of renal function during the immediate newborn period. The organism recovered from both the blood and cerebrospinal fluid cultures was sensitive to streptomycin 6.5 μg./cc.; with the parenteral administration of large doses of dihydrostreptomycin, the concentrations in the blood and cerebrospinal fluid were well above this level.

The passive transfer of antibodies from the mother as well as early diagnosis and treatment probably has contributed to the successful treatment of this patient.

Summary

A case of H. influenzae meningitis in a 4 day old infant is reported in which recovery was obtained without intrathecal medication. Treatment consisted of parenteral streptomycin, sodium sulfadiazine and penicillin.

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SPANISH ABSTRACT

Restablecimiento Sin Terapia Intratecal de un Infante de Cuatro Días de Edad con Meningitis Influenzal

Se reporta un caso de H. influenzae meningitis en un infante de cuatro días de edad en el cual se obtuvo el restablecimiento sin medicación intratecal. El tratamiento consistió en estreptomicina, sulfadiazina de sodio y penicilina parentéricas.

20 South Dunlap Street

677 CONGENITALLY MALFORMED INFANTS AND ASSOCIATED GESTATIONAL CHARACTERISTICS

I. General Considerations

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INTRODUCTION

CONGENITAL malformations are defects which are present at birth. Lay persons have long ascribed them to a multitude of natural and supernatural prenatal influences and the medical profession, hampered by the difficulties of observing human fetal development within the uterus, has long ascribed them to defective inheritance and adopted a fatalistic attitude toward them. Studies in human teratology until recently have been confined largely to descriptions of frequencies and morphologies. Congenital malformations, as an unhappy result, have remained unchanged in incidence while fetal and infant morbidity and mortality due to many other causes have declined.

In 1940, Warkany[1] announced the production of skeletal deformities in rats whose mothers had been reared on a deficient diet. Gregg's report[2] was published the next year and teratology, as an etiologic science, was conceived with this proof that human congenital malformations can result from environmental insult. It is not necessary to summarize here the voluminous literature which has been published since these two papers, and the reader is referred for bibliography to two excellent recent reviews by Gruenwald[3] and Warkany.[4]

Wesselhoeft[5] has named rubella the modern Flibbertigibbet, after Shakespeare's fiend who "squints the eye and makes the hare-lip." He writes, in an article which summarizes the literature on this disease, "The Flibbertigibbet of today responsible for at least some congenital defects seems to be the virus of rubella, which stalks unseen by day as well as by night in the house, the school room and crowded places and which until recently was quite unsuspected and unfeared." Numerous other diseases have been indicted, but only rubella seems to have been convicted. There is danger that the importance of this disease has been magnified unduly and that other factors of teratogenic importance are being obscured as a result. It is well to remember that Wesselhoeft holds it responsible only "for at least some congenital defects" and that Gregg wrote,[6] " . . . I regard rubella and its sequelae as the title of but one chapter in the full story of congenital defects; many more chapters have yet to be written."

Research into the etiology of congenital malformations is made more difficult by the fact that acquired defects, or phenocopies, may simulate inherited defects with great exactness. Furthermore, they may be repeated in members of the same family because the

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same unfavorable environment is at work: familial cretinism and toxoplasmosis are possible examples of this. Inherited defects, on the other hand, may not repeat in the members of a family under observation: they may be inherited as recessive characters and the small size of human samples studied may not reveal them; they may require several abnormal genes for their expression and so be exhibited only rarely; or they may have reduced expressivity and thus cause only a minor abnormality not obvious to casual observation.

Thus, familial occurrence does not always imply an inherited defect and lack of it does not exclude an inherited one. Some malformations, furthermore, may be the result of a defective gene which is allowed to express itself only under certain environmental conditions. It is obvious that it is desirable to distinguish acquired from inherited defects in studying etiology and in giving prognosis, but caution is indicated and "unwarranted oversimplification and generalization are frequent sources of misunderstanding."[4]

Gruenwald, appreciating the difficulties and complexities of research in this field, has suggested the statistical approach.[3] "It is quite possible that in the future many questions of the action of hereditary or environmental influences on the developing organism will be answered by statistical evaluation of large groups of cases. Particularly concerning human maldevelopment, results might be obtained which would otherwise not be available, as experimental methods cannot be used."

The difficulties of the statistical method are several, unfortunately, and these may result in fallacious conclusions:

1. Defects are classified at present on the basis of morphology. This classification is not adequate because a variety of inherited factors and of noxious agents may act on the fetus to produce similar morphologic defects.

2. Many defects are not visible except at postmortem examination or at operation. Samples of dead babies, however, are not random and may result in deductions which are not valid if they are referred to the living population.

3. Adequately sized samples of malformed infants are difficult to obtain except from birth certificates and the latter, with their paucity of pertinent information, usually permit only gross analysis.

4. Comparable control groups are difficult to establish.

5. The statistical method often utilizes questionnaires, which may result in bizarre sampling: the present-day mother of a defective child is tempted to magnify a minor febrile illness during pregnancy.

It seems worth while, nevertheless, to examine the records of a large group of congenitally malformed newborn infants and the obstetric records of their mothers, to compare one type of malformation with another in this series where all cases are selected on the same basis, and thus to attempt to bring out differences in certain associated gestational factors. "The multiplicity of factors discovered . . . may seem confusing at first, but eventually the knowledge of the complexity of the problem will be beneficial."[7]

Material

The obstetric records of all mothers who gave birth to congenitally malformed infants live or stillborn in the Boston Lying-in Hospital during the years 1930 through 1941, together with the pediatric records of their live babies during the neonatal period, have been abstracted and analyzed. Records subsequent to 1941 were not used for 2 reasons: first, because it was felt desirable to use data routinely recorded at a time antedating interest in infectious disease as a teratogenic agent; second, because this review was regarded as a preliminary to vigorous study of current material. Although records dating from the 1918 epidemic of influenza might have proved instructive, it was not possible to include data prior to 1930, for these earlier records were not in convenient form for abstraction.

Each bound record includes a summary of the family, medical, and previous obstetric history of the mother, and her obstetric history for each pregnancy followed in the Boston Lying-in Hospital; thus, data on prenatal examinations dating usually from the third or fourth month of gestation, details of each delivery, and complete pediatric records of the neonatal periods of every infant hospital-born to the mother were available. It is estimated that over 90% of the primiparous and approximately 50% of the multiparous women cared for by the hospital during this period were delivered in the hospital. Very few records of malformed infants were found among home deliveries, possibly because the latter infants were not so thoroughly examined; these babies consequently were excluded from this series.

The series consists of 673 pregnancies resulting in 689 babies born to 662 mothers. Eleven mothers appear twice in the series with 2 malformed infants. Sixteen pairs of twins are included, 32 babies, of which 20 were malformed. Both babies were malformed in 4 twin births, bringing the total number of defective infants to 677.

The 20 malformed twins are excluded from most of the tables which follow in order to avoid a further factor complicating analysis. Twinning occurred approximately 350 times in 29,024 total births, an incidence of 1:83, which is expected. However, twinning with 1 or both infants malformed occurred 16 times in 677 malformed births, an incidence of 1:42 or approximately twice the expected frequency. Although it was not possible to distinguish fraternal and identical twins, it is interesting to recall that monozygotic twins can be produced in animals by damaging the ovum[8] and to theorize that even a fraternal twin might harm its colleague's development by mechanical pressure or by competition for oxygen and nutrients. It is intriguing to note, further, that 7 of the 16 pairs of twins were born in 1941. This has not been possible to explain. Since twinning in itself may represent a malformation or may be associated with a malformation, it might prove instructive to explore environmental circumstances associated with an unusual frequency of twinning in a larger series.

Malformations which were of dubious validity were recorded for 174 of the surviving babies. This group is discussed further in a subsequent section and is excluded from many of the tables to follow.

Racial factors were not analyzed because there were only 18 Negro babies and 1 Chinese baby. Information on sex has not been included because it added little except for the well-known fact that anencephalics showed a ratio of 3 females to 1 male. Five mothers showed serologic tests positive for syphilis; 2 of the mothers were congenital syphilitics and all except 1 were adequately treated. The result of the serologic test was not recorded in 23 pregnancies. No mothers were irradiated during their pregnancies; their history of radiation previous to pregnancy is unknown.

TABLE 1

BOSTON LYING-IN HOSPITAL, 1930–1941

	Total	Malformed Single	Malformed Twin	Malformed Total	Percentage
Births	29,024	657	20	677	2.3%
Stillbirths	787	120	5	125	15.9
Babies dying under 10 days	638	80	4	84	13.2
Babies living	27,599	457	11	468	1.7

Table 1 gives pertinent vital statistics for the series. It should be noted that malformed infants account for a high percentage of the total stillbirths (15.9%) and of the total deaths under 10 days of age (13.2%).*

Maternal clinical data concerning pernicious vomiting, toxemia, prenatal bleeding, anemia, polyhydramnios, acute and chronic disease, and condition of placenta have been analyzed in respect to the various types of malformations. General data concerning the ages of father and mother, the age of mother at marriage, birth order, previous pregnancies and the intervals between them and their outcomes, prematurity on the basis of birth weight and of estimated period of gestation, and seasonal distribution of the pregnancies have been analyzed in respect to these same types and with reference to infectious disease existing in Massachusetts at the time. The limitations of the data are discussed in the sections to follow.

* Henceforth the phrases "deaths occurring under 10 days of age" and "neonatal deaths" will be used interchangeably.

TABLE 2

DEFECTIVE INFANTS CLASSIFIED UNDER SYSTEM AFFECTED

System		Surviving Infants	Neonatal Deaths	Stillbirths	Total with Confirmed Diagnoses
Central nervous	Valid diagnoses; Invalid* diagnoses	80 39	10	95	185
Valid diagnoses					
Pilonidal sinus referred to Children's Hospital		11	0	0	11
Spina bifida		10	0	0	10
Meningocele		8	0	2	10
Meningocele, spina bifida		5	1	2	8
Meningocele, spina bifida, clubfoot		7	1	3	11
Hydrocephalus		11	0	9	20
Hydrocephalus, clubfoot, and other deformities		2	2	1	5
Hydrocephalus, meningocele, spina bifida		9	2	8	19
Hydrocephalus and other deformities		5	0	2	7
Anencephalus		0	0	48	48
Anencephalus, spina bifida and/or meningocele		0	1	8	9
Anencephalus and other deformities		0	1	9	10
Mongolism		12	2	1	15
Invalid diagnoses					
Pilonidal sinus not referred to Children's Hospital		35	0	0	0
Microcephaly		4	0	2	2
Gastrointestinal	Valid diagnoses; Invalid diagnoses	2 10	11	0	13
Valid diagnoses					
Diaphragmatic hernia		1	2	0	3
Tracheo-esophageal fistula		1	3	0	4
Invalid diagnoses					
Incomplete rotation of gut		2	2	0	2
Atresia of gut		8	4	0	4
Musculo-skeletal	Valid diagnoses; Invalid diagnoses	118 72	8	6	132
Valid diagnoses					
1 clubfoot		30	0	0	30
Supernumerary nipple		2	0	0	2
Clubhands, with or without clubfeet		2	1	0	3

* The use of the terms "valid" and "invalid" is perhaps unfortunate. There is no doubt that many of the infants in the so-called invalid group did, in fact, have congenital defects, but it is impossible to determine how many from the information on the records.

TABLE 2—(*Continued*)

System		Surviving Infants	Neonatal Deaths	Stillbirths	Total with Confirmed Diagnoses
Clubfeet and other deformities		8	0	0	8
Achondroplasia		0	2	2	4
Polydactylism		22	0	0	22
Missing extremities		8	0	0	8
Syndactylism		14	0	0	14
Branchial cleft		2	0	0	2
Cleft palate		10	0	1	11
Harelip		6	0	2	8
Cleft palate, harelip		14	0	1	15
Invalid diagnoses					
Bilateral clubfeet		40	2	0	2
Micrognathia		8	0	0	0
Deformities of external ear		7	0	0	0
Miscellaneous skeletal defects		17	3	0	3
Cardiovascular	Valid diagnoses; Invalid diagnoses	42 46	26	2	70
Valid diagnoses					
Congenital heart disease		42	20	2	64
Invalid diagnoses					
Probable congenital heart disease		30	1	0	1
Questionable congenital heart disease		16	5	0	5
Genitourinary	Valid diagnoses; Invalid diagnoses	28 1	1	2	31
Valid diagnoses					
Hypospadias		28	1	0	29
Invalid diagnoses					
Polycystic kidneys		1	0	2	2
Multiple deformities	Valid diagnoses; Invalid diagnoses	13 0	22	13	48
Valid diagnoses					
Specified multiple deformities		13	22	13	48
Miscellaneous	Valid diagnoses; Invalid diagnoses	0 6	2	2	4
Total	Valid diagnoses; Invalid diagnoses	283 174	80	120	483

Classification of Defects

During the period 1930-41 the Boston Lying-in Hospital was using the Classification of Diseases[8] which has been adopted by several Boston hospitals. This classification followed closely the International List of Causes of Death[9] but was modified to fit the purposes of the hospitals. Inspection of the records of the 677 babies showed that approximately 150 terms had been used to describe the malformations. Some of these were, of course, synonyms. Since a list of this length was impractical to use, the diagnoses were combined into a shorter list in which 42 terms were grouped under the system affected. Table 2 shows this detailed list. It gives for each category the number of surviving infants, of neonatal deaths, and of stillbirths. The total number of infants in the table is 657, since the twins are excluded.

It should be obvious that such a procedure is arbitrary and that no two individuals are apt to follow it in the same way. If an infant has more than one defect, and one third of this series did, there is a tendency to classify the infant according to his most severe defect and to place him in the "multiple" category only when he has several severe defects. The resulting classification under systems may therefore be heavily weighted by the lethality of the defects under consideration. While this may be important, there is no reason to believe that lethality is related to etiology. Even if it were possible to refer the defects to the appropriate system or combination of systems in the case of multiple defects, such a classification would not necessarily yield any information about etiology. It is known that a given defect may be the result of a variety of causes; it is known also that a single cause may result in defects in more than one system.

The purpose of this paper is to discuss all the malformations in infants born in the Boston Lying-in Hospital during 1930-1941. It is obviously impossible to determine how many defective surviving infants were not detected at the birth and discharge examinations. This may have been a large number, particularly if minor variations from "normal" are taken into consideration. However, limited discussion of the accuracy of diagnosis of the defects which were discovered is possible.

Murphy's[10] study of malformations was limited to dead individuals on whose death certificates malformations were noted. In order to be included in Murphy's series, an individual had to have a defect visible at birth; or, if the defect was internal, operation or necropsy was necessary before the individual was included in the group of confirmed diagnoses. Table 2 lists 120 stillbirths in the present series of malformations; nearly all of these were examined by the pathology service. Only two of these 120 stillbirths might possibly have failed to fulfill Murphy's definition of a confirmed diagnosis: one had "polycystic kidneys" diagnosed by palpation only, while the other had "multiple anomalies" not further described. Of the 80 neonatal deaths, 52 had autopsies, while 25 had visible defects or defects which were discovered by means of roentgenograph or electrocardiograph. Of the remaining three, one was described as having "malrotation of the mesentery," another as having "malposition of the large bowel," while the third had a "duodenal atresia." It would appear not only that the stillborn and the dead infants can be considered to have confirmed diagnoses but that because of the availability of the pathology service these two groups are reasonably complete. The statement made previously that 13.2% of the dead infants and 15.9% of the stillbirths were found to have congenital malformations gives a reasonably accurate estimate of the importance of congenital malformations in these two groups in this hospital during this period.

In the process of abstracting the records of the malformed surviving infants, it was

noted that some defects were very frequent at certain times. Pilonidal sinus, for example, appeared in epidemic proportions in December 1940 and January 1941, but study of the records disclosed the presence of a pediatric intern with an undue fondness for this diagnosis. Consequently, the infants with pilonidal sinus were separated into two groups. The diagnosis was called "valid" if the infant was referred to the Children's Hospital for treatment of this defect; it was called "invalid" if there was no comment as to the disposition of the infant.

Of the 457 surviving infants in table 2, 174 are listed as having invalid diagnoses. Bilateral clubfeet was considered invalid because 17 of the 40 infants so diagnosed appeared in the year 1941, while the infants in the category of one clubfoot were spread at random over the 12 years. Dunham[11] comments on the inaccuracy of this diagnosis. Other defects in the surviving infants who were placed in the invalid diagnosis category, because of the

TABLE 3

PERCENTAGES OF INFANTS WITH DIFFERENT TYPES OF DEFECTS

System	Surviving Infants with Valid Diagnoses	Neonatal Deaths	Stillbirths
Central nervous	28.3%	12.5%	79.2%
Gastrointestinal	.7	13.8	0
Musculo-skeletal	41.7	10.0	5.0
Cardiovascular	14.8	32.5	1.7
Genitourinary	9.9	1.2	1.7
Multiple deformities	4.6	27.5	10.8
Miscellaneous	0	2.5	1.7
Total	100.0	100.0	100.1
No.	283	80	120

nature of the malformations or the lack of confirmatory evidence, were micrognathia, deformities of the external ears, miscellaneous musculo-skeletal defects, microcephaly, incomplete rotation of the gut, atresias of the gut, cystic kidneys, and miscellaneous defects. The diagnosis of congenital heart disease in surviving infants was considered correct only when substantiated by roentgenogram or the electrocardiograph or when the clinical description was sufficiently detailed and convincing.

Study of table 2 shows, as is well known, that certain of the defects appear frequently in combination. Cleft palate and harelip appear together more often than either appears separately. Meningocele and spina bifida are often together, while both these conditions appear frequently with hydrocephalus and with anencephalus. Clubfoot is frequently associated with other anomalies. The category, multiple deformities, includes 48 infants. This series of observations is not large enough to permit detailed discussion of the association of defects. These infants come from a group of 29,024 births and, consequently, the incidence of a given defect is small. The associations mentioned are probably significant in the statistical sense. The background of information for their interpretation is lacking. Some of the associations may be due to fads in diagnosis. Others may result from the influence of an outside agent(s) acting at a given period of gestation and damaging several parts of the embryo which are developing at that time. Others may be the result of pleiotropism.

Table 2 has been presented in some detail because it brings out a considerable amount of information basic to subsequent discussion. The 42 categories are cumbersome, but it must be remembered that even these are arbitrary to a certain extent.

The percentages of infants with defects listed under seven major headings are given in table 3 for each of the three groups: surviving infants, neonatal deaths and stillbirths. It is immediately apparent that the type of defect found is associated with the status of the infant. Of the surviving infants, 42% have defects of the musculo-skeletal system, while only 10 and 5% of the infants in the other groups are thus affected. Thirty-two per cent of the neonatal deaths have defects referable to the cardiovascular system, while 28% have multiple deformities. Seventy-nine per cent of the stillbirths have defects of the central nervous system. It is possible to compare this series with similar tabulations from the literature,[10, 12] but such comparisons have little meaning since they depend on the method of

TABLE 4

LUNAR MONTHS DURING GESTATION IN WHICH DEFECT PRESUMABLY APPEARED

	Single Mo.				Multiple Mo.				
Mo.	1	2	3	4	1 and 2	2 and 3	3 and 4	More than 2 involved	Total
No. of infants	103	303	49	27	27	102	2	44	657

assigning a defective infant to a particular category and more importantly on the source of the material. Heterogeneous series composed of mixtures of surviving infants, neonatal deaths and stillbirths may be expected to show highly variable percentages of different types of defects. Insofar as can be determined, this series does not differ in an unexpected manner from those in the literature.

Since the classification of defects under the system affected was not entirely satisfactory, it was decided to try other methods of classification. Arey[13] gives a table which shows the development of the different organs according to the age of the embryo. On the basis of this, an attempt was made to determine the lunar month during gestation in which each of the defects in the 657 infants presumably appeared. The infants were then separated into the groups shown in table 4.

The group of infants with invalid diagnoses was included in this table and the twins were excluded. There were 103 infants whose defects presumably developed during the first month of gestation. Some of these infants may have had more than one defect, but such other defects also developed during the first month. There were 27 infants with more than one defect in whom the defects were such as to indicate their development during the first and second months of gestation. Forty-four babies had defects in which the period of development seemed to involve more than two months. On the basis of this classification, 175 infants might be said to have multiple defects in the sense that two or more months during gestation were involved. This method of tabulating the material is experimental, but it is being presented because its use has shown some interesting results which will be presented subsequently. It should be remembered that although a defect may appear during the third month of gestation, for example, the condition(s) responsible for its appearance may have been present at any time previously.*

* An attempt was made to classify the defects on the basis of the germ layers involved. This did not prove feasible.

TABLE 5

COMPARISON OF 2 SYSTEMS OF CLASSIFYING DEFECTIVE INFANTS

System Affected	Mo. During Gestation when Defect Developed								Total
	Single				Multiple				
	1	2	3	4	1 and 2	2 and 3	3 and 4	More than 2	
Central nervous	59	32	27	0	6	40	0	21	185
Gastrointestinal	3	4	4	0	1	0	0	1	13
Musculo-skeletal	0	92	9	0	1	26	0	4	132
Cardiovascular	4	55	0	0	6	4	0	1	70
Genitourinary	0	2	1	27	0	0	0	1	31
Multiple deformities	0	5	2	0	8	17	1	15	48
Miscellaneous	0	1	0	0	2	0	0	1	4
Total	66	191	43	27	24	87	1	44	483

Two methods of classifying the defects have been presented, one traditional and the other experimental. Table 5, based on the 80 neonatal deaths, 120 stillbirths and the 283 surviving infants with so-called valid diagnoses, compares the two systems of tabulation. The table shows that the CNS defects frequently involve several of the months, while defects of cardiovascular and musculo-skeletal systems tend to be concentrated in the second month.

The mortality rates in the various categories of the two classifications are of some interest. Table 6 gives the total mortality, the stillbirth mortality and the neonatal mortality for malformed infants. The total mortality and the stillbirth mortality are based on the total number of births of malformed infants, while the neonatal mortality is based on live born malformed infants. The total mortality is high in the central nervous, gastrointestinal and multiple categories. The stillbirth mortality is high for the CNS defects, while the neonatal mortality is high in the gastrointestinal and multiple categories. Forty-one per cent of the infants live and stillborn with diagnosed congenital malformations died before they were 10 days old. If the group with invalid diagnoses is included, the mortality is 30%.

When the month during which the defects presumably appeared is used as the method of classification, certain trends appear in the mortalities. The mortality is high when the early months are involved and declines as the defects appear later. Where more than one month is involved, the mortalities are higher but again tend to decline when the months are the later ones. This is inherently reasonable and seems in part to justify further interest in this method of classification.

ANNUAL AND SEASONAL DISTRIBUTION

Previous discussion has centered about the material as a whole. General remarks have been made as to the frequency of malformed infants, the classification of their defects and their mortalities. Analysis of the number of defective infants born in the different years of observation is of some importance. If it can be shown that the number of defective infants is significantly large in certain years, it then becomes worth while to search for environmental influences which may have been present in those years. Table 7 presents the

TABLE 6

MORTALITY RATES IN 2 CLASSIFICATIONS

System Affected	Total Infants	Stillbirths	Neonatal Deaths	Total Mortality/ 100	Stillbirth Mortality/ 100	Neonatal Mortality/ 100
Central nervous	185	95	10	57%	51%	11%
Gastrointestinal	13	0	11	85	0	85
Musculo-skeletal	132	6	8	11	5	6
Cardiovascular	70	2	26	40	3	38
Genitourinary	31	2	1	10	6	3
Multiple deformities	48	13	22	73	27	63
Miscellaneous	4	2	2	100	50	100
Total	483	120	80	41.4	24.8	22.0
Mo.						
1	66	48	4	79%	73%	22%
2	191	14	31	24	7	18
3	43	6	4	23	14	11
4	27	0	1	4	0	4
1 and 2	24	7	12	79	29	71
2 and 3	87	19	16	40	22	24
3 and 4	1	0	0	0	0	0
More than 2	44	26	12	86	59	67
Total	483	120	80	41.4	24.8	22.0

material basic to this discussion. The table gives the total number of births (exclusive of abortions), stillbirths and neonatal deaths from all causes occurring in the Boston Lying-in Hospital in each of the years as well as the number of defective infants according to their status. The twins are included in this table. The stillbirth rates and the total malformation rate are based on the total annual number of births in the hospital, while the neonatal mortality rates and the malformation rate of surviving infants are computed from the live births.

Inspection of the table shows that the neonatal mortality rate and the stillbirth rate in the hospital as a whole have declined. No such decline appears in the malformation rates. The total malformation rate, which has as its numerator surviving infants with valid diagnoses, malformed neonatal deaths and stillbirths, has increased, but most of this increase is accounted for by the rate for surviving infants with malformations. This probably reflects a slow improvement in the diagnosis of malformations in live infants. The stillbirth and neonatal mortality rates for congenital defects show no consistent trend, although both rates are highly variable. The annual fluctuations in the stillbirth and neonatal mortality rates for the entire hospital population are not, in general, reflected in the malformation rates. It would be expected that a large increase in the neonatal mortality rate in this hospital due to a cause such as epidemic diarrhea of the newborn infant would be reflected as an increase in the neonatal congenital malformation death rate but would result in a decreased rate for surviving defective infants and no change in the total malformation rate. There was no epidemic diarrhea of the newborn infant in this hospital and fluctuations

from similar causes do not appear in the years studied here. Deaths due to congenital defects comprise only 13% of the hospital's infant deaths; consequently, it cannot be expected that true annual fluctuations in the number of defective infants as evidenced by the small number of deaths will be reflected in the neonatal mortality of the hospital as a whole.

Table 7 indicates that there were four years in which the total malformation rate was high. These years were 1932, 1935, 1938 and 1941. The neonatal malformation mortality

TABLE 7

CONGENITAL MALFORMATION RATES AND TOTAL MORTALITY RATES IN BOSTON LYING-IN HOSPITAL, BY YEAR—1930–1941

Yr.	Total BLiH			Malformations			
				Surviving Infants			
	Births	Stillbirths	Neonatal Deaths	Invalid	Valid	Stillbirths	Neonatal Deaths
1930	1,887	61	53	5	10	8	2
1931	1,873	60	56	8	10	6	3
1932	2,019	55	49	16	27	10	8
1933	2,086	76	59	9	14	11	4
1934	2,415	72	65	11	14	15	7
1935	2,687	69	68	10	29	13	14
1936	2,667	66	43	7	31	6	6
1937	2,606	75	42	10	30	8	5
1938	2,508	52	56	9	32	13	9
1939	2,616	64	44	21	24	11	8
1940	2,716	57	45	20	33	8	8
1941	2,944	80	58	48	40	16	10
	29,024	787	638	174	294	125	84

Yr.	BLiH Stillbirth Rate/1,000	BLiH Neonatal Death Rate/1,000	Malformation Rates/1,000 Births			
			Total (exclusive invalid)	Surviving	Stillbirth	Neonatal
1930	32.3	28.9	10.6	5.5	4.2	1.1
1931	32.0	30.9	10.1	5.5	3.2	1.7
1932	27.2	24.9	22.3	13.7	5.0	4.1
1933	36.4	29.4	13.9	7.0	5.3	2.0
1934	29.8	27.7	14.9	6.0	6.2	3.0
1935	25.7	26.0	20.8	11.1	4.8	5.4
1936	24.7	16.5	16.1	11.9	2.2	2.3
1937	28.8	16.6	16.5	11.9	3.1	2.0
1938	20.7	22.8	21.5	13.0	5.2	3.7
1939	24.5	17.2	16.4	9.4	4.2	3.1
1940	21.0	16.9	18.0	12.4	2.9	3.0
1941	27.2	20.3	22.4	14.0	5.4	3.5
Total	27.1	22.6	17.3	10.4	4.3	3.0

rate was high in 1932 and 1938; it was even higher in 1935. The rate for surviving infants was high in 1932, while the stillbirth rate for defective infants followed a course independent of the other rates. These four years seem to be worthy of special consideration.

In 1935 the number of cases of rubella in Massachusetts was reported to be 33,625. In this series of 12 years the average annual number of cases of rubella was 4,884 and the highest number, excluding 1935, was 6,591. The height of the rubella epidemic was in April, May and June of 1935, and the births of defective infants in the Boston Lying-in Hospital reached a peak approximately seven months later in October, November and December. Thus, analysis of the records collected routinely by the hospital suggests the relationship between rubella and congenital defects. It is important to note that the material was collected at a time when the teratogenic properties of this virus were unknown, and consequently that it was not subject to the bias which may complicate information currently being gathered in studies of the association of rubella and other communicable diseases with congenital malformations.

Because the 1935 peak in the number of defective infants could be accounted for in a logical fashion, explanations of a similar nature were sought for the years 1932, 1938 and 1941. The numbers of defective infants born in the different months of these three years did not reach pronounced peaks as they did in 1935; the evidence for an outside agent(s) is therefore not so clearcut. Table 8 lists the years in which certain of the reportable

TABLE 8

HIGH YEARS FOR CERTAIN COMMUNICABLE DISEASES IN MASSACHUSETTS

Rubeola	Rubella	Poliomyelitis	Scarlet Fever	Epidemic Parotitis	Varicella
1930	1935	1931	1932	1932	None
1934		1935	1938	1936	
1936				1941	
1939					

communicable diseases reached high levels in Massachusetts. Although some of the diseases, poliomyelitis, scarlet fever and mumps, were at high levels in the years when the number of defective infants was high, it is not suggested that these diseases can be incriminated on the basis of this evidence. Study of the material, however, indicates a method of attack on the problem of congenital malformations which can be used more effectively than it has been in the past. Comparable studies in several of the large maternity hospitals will indicate which of the acute communicable diseases should be further considered.

Study of the years in which the number of defective infants was high suggests that certain of the acute communicable diseases cannot be entirely dismissed from further consideration. The more general problem of the seasonal distribution of births of defective infants was also studied in order to determine if there were indications that the defective infants were in an early stage of their embryonic development at a season when respiratory disease was high. Because the number of infants born in any one month was small, the months have been combined into quarters of a year. Table 9 gives the quarter of the year in which each of the 483 defective infants was born. The group with invalid diagnoses and the twins are omitted. There is no significant seasonal variation in the total or in any of the three groups of surviving infants, neonatal deaths and stillbirths.

TABLE 9

BIRTHS OF DEFECTIVE INFANTS ACCORDING TO SEASON OF YEAR

Quarter of Birth	Surviving Infants Valid Diagnoses	Neonatal Deaths	Stillbirths	Total	Quarter of Conception
1st (Jan., Feb., March)	71	17	25	113	2nd
2nd (April, May, June)	59	19	34	112	3rd
3rd (July, Aug., Sept.)	80	19	36	135	4th
4th (Oct., Nov., Dec.)	73	25	25	123	1st
Total	283	80	120	483	

It is not surprising that a significant seasonal distribution in the total group was not found. Respiratory disease in general would not be expected to play a role in all types of congenital defects, the causes of which are legion. Therefore, an attempt was made to determine if a group of infants could be found whose births showed significant seasonal variation. Classification of the defects according to system affected (table 2) isolated no such group. An interesting result appeared, however, when the method of classification proposed in table 4 was used. Table 10 gives the number of births in each quarter of the

TABLE 10

SEASON OF BIRTH OF 156 INFANTS WITH MULTIPLE DEFECTS ACCORDING TO MONTH-DURING-GESTATION CLASSIFICATION

Quarter of Birth	Surviving Infants Valid Diagnoses	Neonatal Deaths	Stillbirths	Total	Quarter of Conception
1st	15	9	7	31	2nd
2nd	11	6	9	26	3rd
3rd	20	12	21	53	4th
4th	18	13	15	46	1st
Total	64	40	52	156	

year for the 156 infants with more than one defect which presumably developed over a period of two or more months during gestation. In the total group and in each of the three subgroups the number of births of defective infants in the third and fourth quarters is consistently high. The results are significant in the statistical sense for the stillbirths and for the total group; they are of sufficient interest to suggest that an attempt should be made to confirm them.*

Conclusions from this section of the paper will be presented at the end of Part II. It

* Neither respiratory nor communicable disease can be incriminated as a cause of congenital defect on the basis of this evidence. In a series of this size, it is possible to tabulate the infants in innumerable ways. It is the nature of statistical inference that 5% of such tabulations, if that is the significance level chosen, will be called significant. They may be only those rare events which must occasionally occur by chance. Therefore, speculation as to the meaning of these results is not given.

may be noted here that the records of a large maternity hospital are helpful in studying the etiology of congenital defects.

(This is Part I of the article "677 Congenitally Malformed Infants and Associated Gestational Characteristics." Part II will appear in the August issue of PEDIATRICS.)

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FAVISM IN TWO CHILDREN IN CALIFORNIA

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THAT an acute illness results from the ingestion of fava beans in some individuals was alluded to in the writings of antiquity. Favism was mentioned by Herodotus in the fifth century B. C. In more recent times the condition has been studied and many hundreds of cases reported by Italian writers.[1]

Favism is an acute hemolytic episode with fever and malaise, followed by hemoglobinuria, jaundice and severe anemia, resulting from the inhalation of the pollen or ingestion of the bean of Vicia faba (broad bean, Italian bean, horse bean, fava bean). The disease is most prevalent in Sicily, Sardinia and Calabria where the broad bean is an important staple in the diet. Formerly it was thought that the disease was peculiar to individuals of Italian extraction; however, reports have recently appeared of cases occurring in other parts of the world and in other peoples. Seven cases of favism have been reported in the United States, four of these in children.

Josephs' case[2] was that of a 4 year old boy of Greek parentage residing in Baltimore, who had an acute hemolytic reaction two days after a meal of broad beans. One month after the onset of his attack, the blood had returned to normal and a second attack was precipitated by feeding the boy fava beans.

The other three children were of Italian parentage. The case reported by Wharton and Duesselmann[3] was that of a 3½ year old New York boy, who developed hemoglobinuria and marked weakness the day after a meal of fava beans. There was no family history of similar occurrences.

Rosen and Scanlan[4] reported the case of a 5 year old boy, residing in Rhode Island, who had his attack the day after eating four plates full of broad beans. Further questioning of the parents revealed that the child had had a similar attack two years previously after eating the same type of bean.

Lecks[5] recently reported the occurrence of favism in a 4 year old Pennsylvania child, who had eaten raw fava beans the day before the onset of symptoms. This child's grandmother gave a history of repeated attacks of jaundice after eating fava beans. She also stated that her small son and daughter died shortly after eating this type of bean.

McCrae and Ullery[6] reported the occurrence of a case in Philadelphia in a man 53 years old. This patient had been born in Italy and gave a history of similar attacks during his childhood in Sicily. Following his recovery a skin test with extract from fava beans was positive and was followed by mild symptoms of favism.

Hutton's patient[7] was an Italian-born resident of New York, 21 years of age, who had an attack after eating a dish of fava beans. Many of this man's relatives had suffered similar episodes and one of them had died of an attack of favism.

Eads and Kash[8] reported the case of a sailor of Spanish-Jewish ancestry, who was admitted to a United States Naval Hospital in shock and proved to have favism. A skin test performed after his recovery was positive.

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Case Reports

Case 1. L. G. C. was a 3 yr. old child, who had been in excellent health until May 27, 1948, when the parents noted that he looked a little pale, but was otherwise lively and in apparent good health. On the following day he became acutely ill with persistent vomiting. He was seen by a local physician, who made a diagnosis of acute food poisoning. During the subsequent 24 hr., the child became extremely pale, deeply jaundiced and somewhat cyanotic. During this period he passed what was described as "black urine." The child was admitted to a hospital in Santa Rosa, Calif., and on admission was found to be an extremely pale, jaundiced, cyanotic child in extremis. Lungs and heart were normal. The abdomen was soft and there was no palpable liver or spleen. Temperature was 37.1°C., pulse 140, respirations 24. A blood count on admission was reported to show WBC 61 thousand/cmm., RBC 1.0 million/cmm. and Hgb. 20% (Sahli). Nucleated red blood cells were noted in the smear. Urinalysis revealed no sugar, 4+ albumin and 4+ hemoglobin reaction. No abnormality of the red blood cells was reported. A diagnosis of acute hemolytic anemia was made. During the next several days the child was given repeated transfusions to a total of 1,000 cc. of whole fresh blood. He was placed in an oxygen tent during the 1st 2 days and was given large doses of penicillin on an empiric basis.

He made a rapid recovery under this treatment and on the 2nd day in the hospital his urine became normal without albumin or hemoglobin. By the 5th day he seemed entirely well. He was discharged from the hospital on the 7th day and referred to San Francisco for further study.

The past history of this child revealed that he was born in Berkeley, Calif. The birth and early development were normal. His only previous illnesses consisted of frequent bad colds and a middle ear infection in 1947.

The family history was not remarkable. The mother and father were living and well and there were no siblings. No family history of any hemolytic disease or jaundice could be elicited. The family had lived in this country for several generations and, as far as could be determined, none of the forebearers were of Italian origin.

The child was first seen by the author on June 8, 1948, at which time he was found to be an essentially normal 3 yr. old child with a negative physical examination. Blood studies at this time revealed RBC 5.4 million/cmm., with Hgb. 16.3 gm./100 cc. WBC was 15.3 thousand/cmm. with a normal distribution. There were 500,000 platelets and 0.2% reticulocytes. Van den Burgh reaction was direct, negative; indirect, 0.3 units. Icterus index was 2 u. Fragility test showed initial hemolysis at 0.46% saline and complete hemolysis at 0.28% saline and complete hemolysis at 0.28% saline. Red cells were not abnormal in morphology.

After the blood studies were completed a further investigation into the history was made and it was found that on May 25, 26 and 27 the child had had broad beans for his supper. These beans were grown by his grandfather in the backyard and were eaten by the entire family during these 3 days. They had previously had a crop of the same beans the previous May, and during that time the child had eaten them on several occasions during the month of May and early June without disturbance. During the intervening year he had had no beans of this type in his diet. A sample of the beans from the grandfather's garden were identified by the Department of Agriculture at the University of California as Vicia faba.

Three months after the hemolytic episode, both scratch and intradermal tests with an extract of fava beans proved to be negative.

Case 2. K. K. was a 2½ yr. old Greek-American child, who had resided in San Francisco since birth. She first became ill on the evening of May 2, 1949, at which time, she complained of malaise and of a headache. Because of her general listlessness and lack of appetite the mother put her to bed early. The next morning it was noticed that the child was deeply jaundiced, but had no other complaints. The headache was gone and she felt well. During the morning the child had 2 bowel movements, which were normal in color and consistency. She urinated several times, but the mother did not notice the color of the urine. She was not nauseated and ate a normal breakfast and lunch. Because of the deep jaundice she was brought in for examination that afternoon.

On examination she seemed active and well, but was very deeply jaundiced. Temperature, pulse and respirations were normal. Upper respiratory passages were clear. Heart and lungs were not remarkable. Neither the liver nor the spleen was palpable. Blood count revealed an erythrocyte count of 2,950,000; Hgb. 8.09 gm./100 cc.; leucocyte count 20,000, of which 65% were neutrophils, 1% eosinophils, 27% lymphocytes and 6% monocytes. There was anisocytosis, polychromasia and reticulocytosis without normoblastosis.

Approximately 18 hr. after the first blood count and with no intervening therapy, RBC had risen to 3.4 million/cmm. with Hgb. 9.48 gm./100 cc. and the reticulocyte count was 136 thousand/cmm. or 4% of the erythrocytes. At this time the child was still feeling quite well and the degree of jaundice had diminished. Three days later, the child had lost her jaundice, but was quite pale. Hgb. at this time was 9.0 gm./100 cc. She was started on a high iron and liver diet and was given ferrous sulfate.

Further questioning of the parents revealed that on the night of May 1, just 24 hr. before the onset of the symptoms, the child had eaten broad beans for supper. This was the first of this season's broad bean crop, which the parents had raised in their own garden. The child's only previous contact with the beans was 1 yr. previously, when she had had them served to her on several occasions during the month of May without disturbance. The beans were seen and identified as Vicia faba.

It is of interest that the child's mother states that she has had several episodes of jaundice in the past few years without knowing the cause.

Discussion

An attack of favism may come on in a sensitized individual after ingestion of raw or partially cooked beans or it may strike shortly after passing through a field in which the plants are flowering. Fortunately, the pollen of the broad bean is sticky and heavy and, therefore, poorly disseminated beyond the field.

The onset of the attack is sudden and without premonitory symptoms, beginning often with a dizzy spell, followed by vomiting, diarrhea and complete prostration. Hemoglobinuria appears within 24 hours, the urine becoming red-brown to black in color. Chills and fever may be present. Jaundice appears within a few hours and may be accompanied by enlargement of the liver and spleen. The red blood cell count during an attack may fall to one million or less, with anisocytosis, poikilocytosis, polychromatophilia and erythroblastosis. The hemoglobin may fall to as low as 10%. A prompt reticulocyte response is usually noted in those patients that do not succumb within the first day or two. There is great variation in the severity of the attacks, the two cases presented here being examples of a severe case with recovery and of a mild case.

In Luisada's review[1] of the extensive Italian literature on favism, he concluded that the allergic theory was generally favored over bacterial or toxic action as an explanation of this disease. Many of the patients tested showed skin sensitivity to fava bean extracts. The severity of the attack was not dependent on the quantity of the beans eaten, but appeared to be related to the degree of individual sensitivity. Some desensitization seemed to occur since most persons had less severe attacks as they grew older. Lecks was unable to demonstrate definite sensitization by skin tests, passive transfer experiments or precipitin reactions, during five months' observation of his patient. He suggested that the patient might still have been in a refractory or anergic phase of tissue response.

In both of the present cases it will be noted that the patients had eaten broad beans a year previously with no resulting disturbance and that during the year had eaten no beans of this type until just before the onset of symptoms. This coincides with the experience of others and fits the picture of sensitization well.

These two cases of favism are the eighth and ninth to be reported in the United States and are the first in the western part of this country. However, more such cases may be expected, especially in California where broad beans are widely grown and are finding ever increasing popularity in the diet, especially among persons of Italian descent, many of whom grow the beans in their own yards.

Since spontaneous recovery occurs in most attacks of favism, and since the etiology of the attack is not evident unless the history is taken with favism in mind, many instances of

this condition may have passed as unexplained jaundice, Lederer's anemia or catarrhal jaundice.

Further study of future cases of favism by more extensive hematologic and immunologic technics now available may well lead to better understanding of the entire group of acute hemolytic anemias, as well as explaining better the exact mechanism of this interesting disease.

Conclusion

The first two instances of favism recognized in the western United States are reported. Attention is called to the widespread use of fava beans in this area and the possibility of favism as a cause of unexplained cases of acute hemolytic anemia or jaundice.

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Spanish Abstract

Fabismo en Dos Niños en California

El fabismo es un episodio agudo hemolítico con fiebre y malestar seguidos de hemoglobinuria, ictericia y severa anemia, que resulta de la inhalación del polen or la ingestión del haba cruda, Vicia Faba. Esta enfermedad es más prevaleciente en Italia y Sicilia; sin embargo, siete casos han sido registrados en los Estados Unidos. Este informe agrega dos casos más que ocurrieron en dos niños en California donde el haba faba o sea un haba ancha se está volviendo popular como alimento.

2201 Webster Street

PHYSIOLOGIC AND CHEMICAL RESPONSE OF PREMATURE INFANTS TO OXYGEN-ENRICHED ATMOSPHERE

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IT HAS long been recognized that prematurely born babies, as well as normal newborn infants, have gross irregularities in rate and amplitude of breathing.[1-5] Various factors have been considered as causes, such as immaturity of the respiration centers of the premature infants,[6] defective development of the alveoli or of the capillary bed in the lungs[7] or of the central nervous system,[8] and differences in blood hemoglobin.[9]

In an attempt to determine how consistently the respiratory centers of premature infants respond to the stimuli of carbon dioxide excess, "oxygen lack" and oxygen excess, Wilson et al.[10] studied a series of 33 premature babies. Twenty-three of 28 babies, while breathing in an atmosphere of high oxygen content, showed a "fairly prompt cessation of the periodic breathing and a change to relatively regular and often somewhat deeper breathing." They were unable to detect any correlation between age and weight and the respiratory pattern of these prematures. These authors were of the opinion that "periodic breathing is best explained by lack of effective hydrogen ion stimulus of a low oxygen atmosphere to act on the carotid sinus." They were also of the opinion that "the fact that any effect on breathing could be produced by administration of a high oxygen atmosphere demonstrated that the average amount of alveolar oxygen had not been sufficiently high to keep the arterial hemoglobin at its usual state of near saturation with oxygen." The authors felt that "any effect from the administration of oxygen establishes that the preceding alveolar oxygen content has not been normal, or that abnormal conditions of gas diffusion in the lungs exist."

PURPOSE

Therefore, it became the purpose of this report to answer the following questions which are logical sequelae to the previous work just mentioned:

1. What is the arterial oxygen saturation of premature babies when in atmosphere and greater concentrations of oxygen?

2. What happens to the character of the breathing and the alveolar ventilation when oxygen is administered in various concentrations to premature babies?

PROCEDURE

A total of 44 premature infants were administered oxygen with temporal artery blood samples obtained before oxygen administration and with various concentrations. On 19 of these 24 patients, continuous plethysmographic recordings were obtained on 29 different occasions. These patients ranged in age from 1 to 65 days and in weight from 1.1 kg. to 2.3 kg.

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The infants were placed in the plethysmograph within a few minutes after being fed so as to assure a quiet period of observation. Recordings were first made while the infants were breathing room atmosphere, then the concentration of oxygen administered was gradually increased. A small plastic hood (Fig. 1-D) was used for this purpose, supplied with oxygen from a nearby oxygen tank. The oxygen concentration being breathed was determined by a Beckman Oxygen Analyzer (Fig. 1-E) with an accuracy within 2%, and the movements of an attached Krogh spirometer were recorded by means of a light source (Fig. 1-A), photo-electric cell (Fig. 1-B) and continuous galvanometer-recorder (Fig. 1-C). Thus, continuous recordings of respiration of these infants were made possible over a protracted period of time. Any change in respiration could then be continuously plotted against

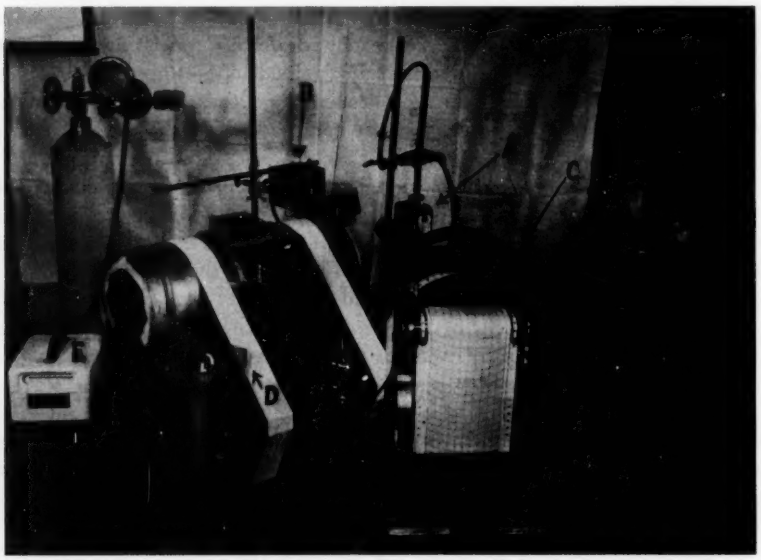


FIG. 1. Plethysmograph and accompanying apparatus used in study.

the concentration of oxygen being administered. Shortly before the plethysmographic tracings were made, arterial blood samples were obtained under conditions similar to those just described except that the infant was fasting.

METHODS AND TECHNICS

Sampling Technic:[11] A 5 ml. syringe was filled with 5 ml. heparin (40 mg./100 ml. solution) and dried in vacuo. A drop of heparin solution was placed on the tip of a plunger which was also dried in vacuo. The plunger of the syringe was coated with light mineral oil (USP) and inserted into the barrel of the syringe. A sharp 22 ga., 1 inch, long bevel needle was attached and sealed to the tip of the syringe by collodion. The temporal artery was palpated and observed for pulsations anterior and forward of the external ear. The artery was usually felt to pulsate for a distance of 1-2 cm. Arteriopuncture was done and 3 ml. of blood withdrawn into the syringe after which any small bubble of trapped air was expelled. The needle was then replaced with a rubber serum bottle cap, and the syringe was rotated to insure mixing with the anticoagulant. Blood samples were placed in an ice bath immediately after they were drawn.

Oxygen content of arterial blood was determined according to Van Slyke.[12] A blood sample of 0.2 ml. was employed.

For the measurement of oxygen capacity of blood the sample was rotated with 10 times its volume of air, in the syringe with which the sample was taken, for at least 20 min. Then the oxygen content was determined in the same manner as that before the sample was aereated. Oxygen saturation was calculated by the following formula:

$$\% \text{ O}_2 \text{ saturation} = \frac{\text{vol. \% O}_2 \text{ content}}{\text{vol.\% O}_2 \text{ capacity}} \times 100.$$

Hematocrit was determined by the Van Allen[23] method using heparinized blood.

Results

Qualitative Analysis of Breathing Records: The breathing of the premature babies was classified by the type of breathing they exhibited in atmosphere and as illustrated diagrammatically in chart 1; thus, Type I includes all those infants breathing periodically with

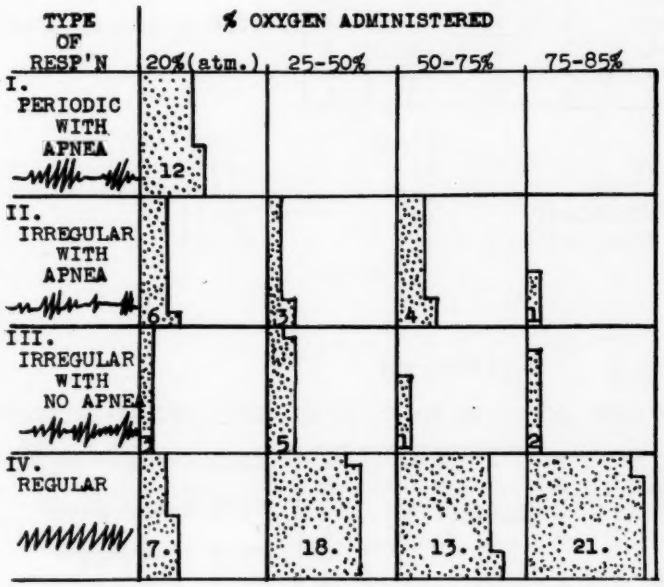


CHART 1. Numerals in stippled area indicate number of infants in this group.

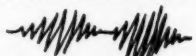
periods of apnea interspersed ("Cheyne-Stokes" type of breathing); Type II represents those breathing irregularly with occasional periods of apnea; Type III includes only those breathing totally irregularly with no periods of apnea; and Type IV includes those individuals with the more regular "adult-type" respiration. Forty-four per cent of the group had periodic breathing in atmosphere (Type I), 25% had regular breathing (Type IV), 21% breathed irregularly with occasional apnea (Type II), the remaining 10% having totally irregular breathing (Type III). Chart 1 illustrates the distribution of type of breathing in these infants when exposed to different concentrations of oxygen. Thus, when 25-50% oxygen was administered, 69% of the group then had regular respiration (Type IV), none had periodic breathing, the remainder fell about equally in the other 2 groups, i.e., irregular, and irregular with occasional apnea. A few more shifted to regular breathing when the concentration of oxygen was increased to 50-75% and, when oxygen administered was 75-85%, 88% of the group then breathed regularly.

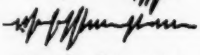
Charts 2-4 and table 1 are a further breakdown of the type of breathing exhibited by

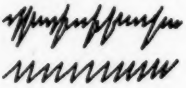
TYPE 1 % OXYGEN ADM.

PATIENT	20	25-50	50-75	75-85
DO	1	4	4	4
JO	1	4	4	4
SA	1	4	4	4
WA,B.	1	4	4	4
CA	1	4	4	4
DO	1	4	4	4
BU	1	4	4/3	4
O'D	1	4	4	-
O'D	1	4	-	-
JA	1	3	4	4
WA,C.	1	3	2	4
BU	1	3	3	4

RESPIRATORY PATTERNS

TYPE 1 

TYPE 2 

TYPE 3 

TYPE 4

	AVERAGE	RANGE
AGE	21	5-57
WEIGHT	3-8	2-8 to 4-8
HEMATOCRIT	45	30-55
ART.% SAT'N.	92	81-97

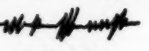
CHART 2.

TYPE 2 % OXYGEN ADM.

PATIENT	20	25-50	50-75	75-85
FI	2	4	4	4
VA	2	4	4	4
ME	2	4	4	4
DA	2	2	4	4
CA	2	2	2	4
JO	2	3	3	4

RESPIRATORY PATTERNS

TYPE 1

TYPE 2 

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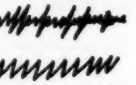
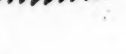
TYPE 3 

TYPE 4 

	AVERAGE	RANGE
AGE	17	4-32
WEIGHT	4-8	3-2 to 5-1
HEMATOCRIT	40	32-47
ART.% SAT'N	94	93-97

CHART 3.

TYPE 3 % OXYGEN ADM.

PATIENT	20	25-50	50-75	75-85
CA	3	4	4	4
DA	3	3	4	4
LO	3	3	3	3

	AVE	RANGE
AGE	9	2-19
WT.	4-0	3-14-4-4
HCT	44	35-64
02 %	88	83-92

CHART 4.

the individuals in each group as classified by their respiratory pattern in atmosphere and in higher oxygen concentrations.

Of the 12 individuals with Type I (periodic) breathing in atmosphere, nine changed to Type IV (regular) breathing when oxygen administered was raised to 25-50%, one when oxygen was raised to 50-75%, and all were breathing regularly (Type IV) when 75-90% oxygen was administered.

Of the six individuals with Type II respiration (irregular with occasional apnea) in atmosphere, three breathed regularly (IV) when 25-50% oxygen was administered, four

TABLE 1

Type 4	% Oxygen Adm.			
Patient	20	25–50	50–75	75–85
JA	4	4	4	4
WA	4	4	4	4
O'D	4	4	4	4
McC	4	4	4	4
MO	4	4	4	4
SM	4	4	4	4
CI, P.	4	4	4	2

	Ave.	Range
Age	25	2–65
Wt.	4–5	2–13/5–0
Hematocrit	45	32–66
Art. % Sat'n	92	82–99

when oxygen was raised to 50-75%, and all breathed regularly in 75-90% oxygen.

Of the three individuals breathing irregularly with apnea (Type III) in atmosphere, one was breathing regularly in 25-50% oxygen, two in 50-75% oxygen. One of these babies (Baby L) revealed no change in respiratory pattern in any increase of oxygen administration.

All the seven individuals who breathed regularly (IV) in atmosphere continued the same type of respiration in 25-50% and 50-75% oxygen. All continued breathing regularly in 75-90% oxygen except one individual who changed to irregular respiration with occasional apnea.

Chart 5 reveals the changes in arterial oxygen saturation with various concentrations of oxygen administered. While in room atmosphere 27 infants had an average arterial oxygen saturation of 93%. Arterial saturation rose to 100% with 70-79% oxygen administered and to an average of 102% with 80-89% oxygen administered. The 102% saturation represents, no doubt, at least 2% of the oxygen being carried by the plasma.

When various age groups were compared (chart 6), it was found that age group I (1-14 days) had an average arterial oxygen saturation of 102.5% in comparison to group II (14-65 days) which saturated to 100.5% with oxygen administration. It should be noted in chart 6 that there was a simultaneously higher hematocrit in group I.

Also, when comparison was made between weight groups, the same findings were noted. The lesser weight groups had higher arterial oxygen saturation when oxygen was administered, despite approximately equal initial saturation. Again, hematocrit levels are higher in the lesser weight groups (see chart 7).

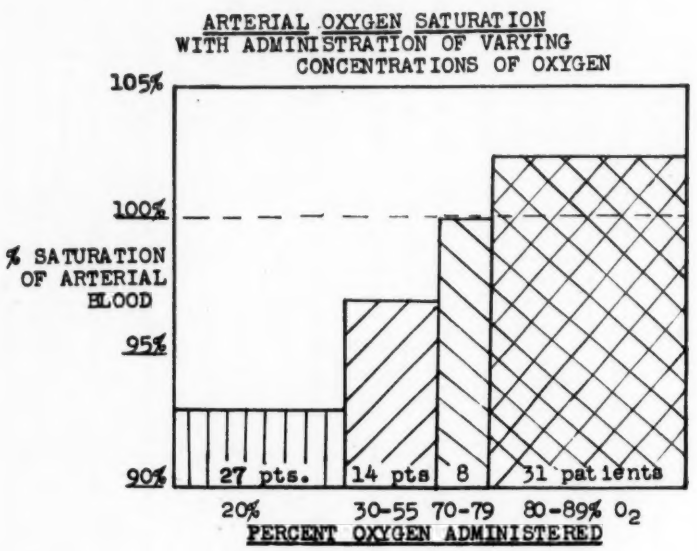
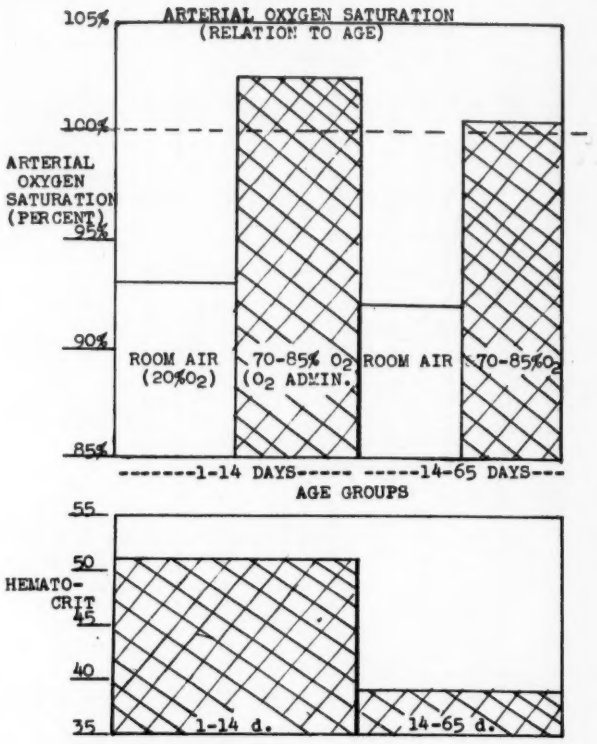
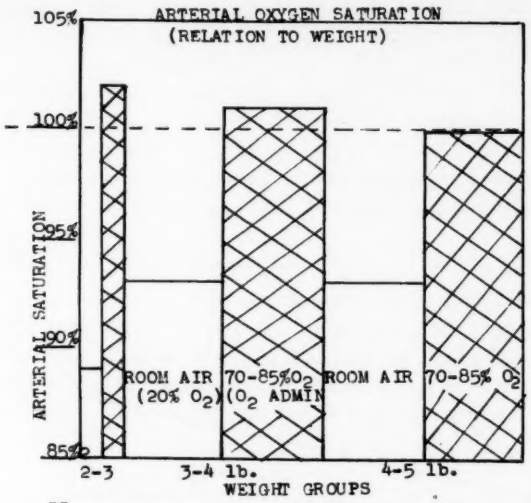


CHART 5.



AGE	(ARTERIAL SATURATION) ROOM AIR	70-85%O_2	HEMATOCRIT	PATIENTS
1-14d.	93%	102.5%	51	22
14-65d.	92%	100.5%	39	17

CHART 6.



WEIGHT	ART.SATURATION R'M AIR	70-85%O_2	HEMATOCRIT	PATIENTS
2-3 lbs	89%	102%	49	4
3-4 lbs	93%	101%	47	18
4-5 lbs	93%	100%	45	19

CHART 7.

It was established by Haldane and associates[14] with adults that 0.3% increase in alveolar carbon dioxide could increase alveolar ventilation by 100%. It is also stated that 1/20 of this amount will noticeably affect alveolar ventilation. Chart 8 represents Haldane's data with carbon dioxide percentage in the inspired air plotted against carbon dioxide percentage in alveolar air and again against "rates of alveolar ventilation." It will be noted that increases in alveolar carbon dioxide are not directly proportional to carbon dioxide inspired. Nor is the relative rate of alveolar ventilation directly proportional to carbon dioxide inspired.

With this in mind it was thought best to determine the carbon dioxide content of the oxygen mask when oxygen was being administered at different speeds and concentrations. A 10 day old, 3.2 kg. child was used as the subject. The oxygen mask employed in this problem was the same used as in the series of experiments with the plethysmograph. Air samples collected were analyzed for carbon dioxide by the method of Van Slyke, Sendroy and Liu.[15]

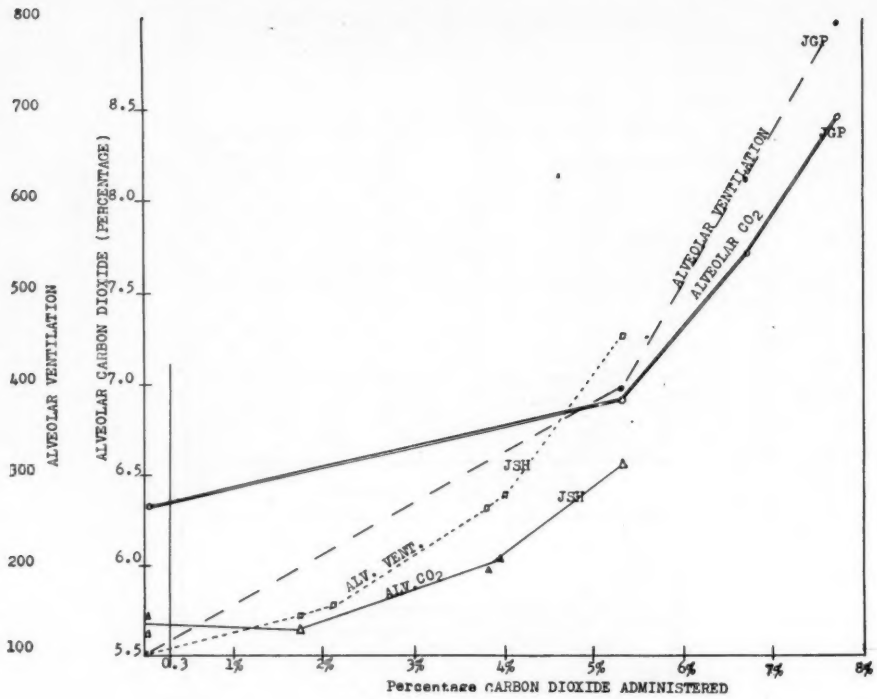


CHART 8.

The data obtained are illustrated in table 2.

TABLE 2

Amt. Oxygen Administered	Oxygen Concentration in Mask	CO_2 Concentration in Mask
1½ l/m	38%	0.31
2 l/m	58%	0.32
4 l/m	60%	0.31
5 l/m	64%	0.27
12–14 l/m	70%	0.093
2 l/m	36%	0.033 no pt. in mask
Atmosphere		0.031

It is evident, using Haldane's data, that 0.3% carbon dioxide in the inspired air does not significantly alter the alveolar carbon dioxide in adults nor does it raise the relative rate of alveolar ventilation beyond 5-10%.

Quantitative Analysis of Breathing Records

Breathing records were quantitated by measuring (from representative sections of each record) and totaling the actual heights of each inspiration as recorded graphically on the drum over a measured time interval.

The interpretation of these records in units of length cannot be taken as a direct and comparable measurement of volume change in respiration of different infants because of (1) individual differences in ratio of dead space to body volume in the plethysmograph and (2) differences in fit and tension of the neck diaphragm. Thus the record of each premature infant was taken as he breathed air as a baseline for study of his response to other concentrations of oxygen.

Any reference in the future to a percentage increase or decrease in rate, minute volume or tidal volume refers to the relative change from 1.00 (as determined for each baby in atmosphere).

Minute Volume

The average minute volume of the group rose 30% when 30-40% oxygen was administered. This level of increased minute volume was maintained until oxygen being administered was raised to 80-90% at which time the increase minute volume was 25%. These averages are found to be significant at the 1% level when subjected to statistical analysis. There is no explanation offered at present for the more aberrant determinations. (See chart 9.)

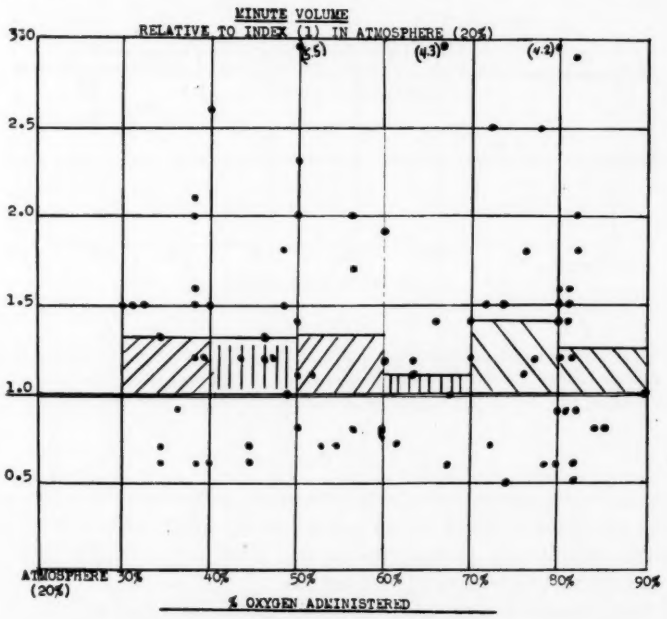


Chart 9.

Note: Each dot represents an individual determination. The height of the hatched column represents the average change for the individuals represented in that area. Abscissa represents % change in minute volume, e.g., 1.5 = 50% above base line, 2.0 = 100% above base line, etc.

Rate

A 30% increase in rate for the group when 30-40% oxygen was administered was found. An increase of 20% over resting value was then maintained until oxygen administered reached 70%. When 70-80% oxygen was given the average increase in rate was less

than 10%, and the rate returned to the original value when 80-90% oxygen was administered.

Despite the apparent spread (range) of individual values these figures are statistically significant. The 30% rise in rate when 30-40% oxygen is administered is significant at the 1% level. The rise of 25% in rate when 40-50% oxygen is administered is significant at the 2% level. The return of rate to normal is again significant when 70-80 and 80-90% oxygen was administered. (See chart 10.)

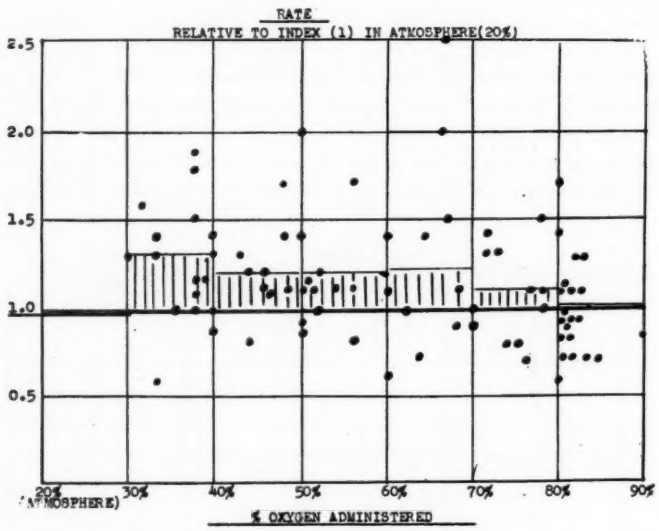


CHART 10.

NOTE: Each dot represents an individual determination. The height of the hatched column represents the average change for the individuals represented in that area. Abscissa represents % change in minute volume, e.g., 1.5 = 50% above base line, 2.0 = 100% above base line, etc.

TIDAL VOLUME

The relative tidal volume rose to an increase of 35% when 70-79% and 80-90% oxygen was administered. There was no increase in tidal volume until 50-60% oxygen was administered when a 16% average increase was noted, followed by a 20% increase in 60-70% and the 35% increase in 70-90% oxygen.

Again, these changes in tidal volume as plotted against the values obtained when patient was breathing atmosphere are significant statistically. (See chart 11.)

One can reason that changes in relative tidal volume, relative minute volume and relative rate are due to oxygen therapy and apart from the very slight accumulation of carbon dioxide in the mask. It seems highly improbable that this significant change in alveolar ventilation could be secured from the effect of carbon dioxide which in adults is inferred as ineffective. Further work with regards to administration of fractions of 1% of carbon dioxide to inspired air might be pertinent and informative. Hence, it is now in progress.

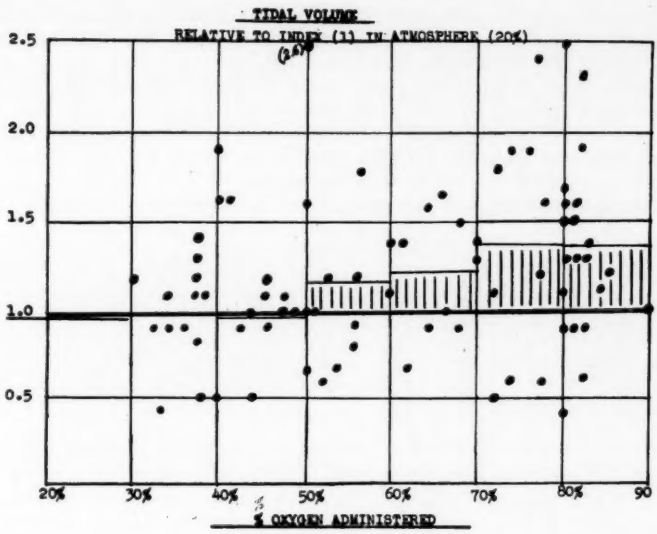


CHART 11.

NOTE: Each dot represents an individual determination. The height of the hatched column represents the average change for the individuals represented in that area. Abscissa represents % change in minute volume, e.g., 1.5 = 50% above base line, 2.0 = 100% above base line, etc.

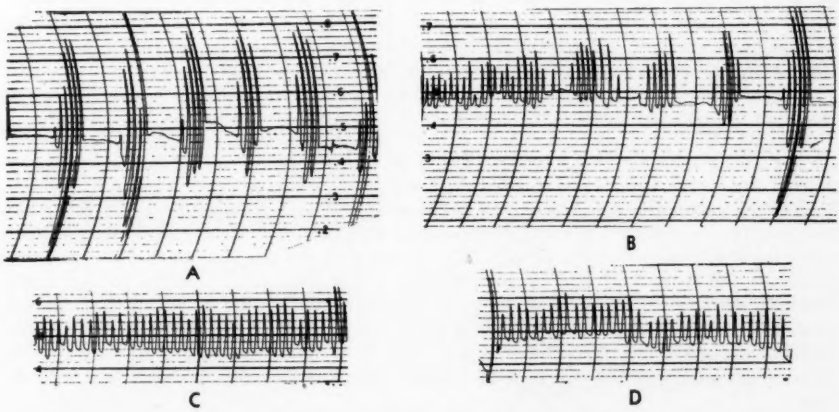


CHART 12 A. (All breathing records read from right to left.) During 16th min.—breathing atmosphere. Periodic, Cheyne-Stokes breathing in atmosphere. B. During 18th-19th min.—infant breathing 36% oxygen. Note transition from periodic type breathing to regular respiration. C. During 28th min. —breathing 50-55% oxygen. Regular respiration. D. During 33rd min.—breathing 78% oxygen. Regular respiration with expiratory lag.

ILLUSTRATIVE CASES

Breathing records and clinical summary of representative individuals from each group are presented in charts 12 to 15. All recordings of respirations were continuous; samples shown are most representative, extracted from the continuous record.

Type I (Periodic breathing with periods of apnea): B. A. W. (see charts 12A-D), 14 day old white girl infant. Wt. 1.5 kg. Birth wt. 1.5 kg. Mother 36 yr. of age, para 4, gravida 5. Premature rupture of membranes 1 mo. prior to EDC, NSD, labor of 22 hr. Temperature stabilized on the 10th day, vitamin supplement started on 12th day. Blood transfusion on 15th day. The baby was immediately quiet and asleep when placed in the plethysmograph.

Type II (Irregular breathing with occasional apnea): V. A. (see charts 13A and B), 27 day old,

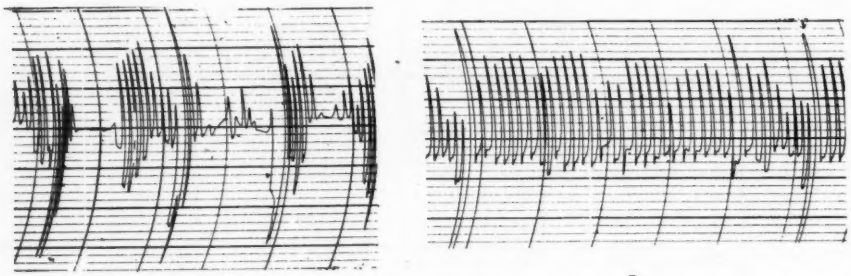


CHART 13 A. During 17th min.—breathing atmosphere. Respiration periodic in type, irregular with interspersed periods of apnea. B. During 32nd min.—patient breathing 86% oxygen. Respirations regular in character. Note expiratory pause.

white male infant. Wt. 2.2 kg. Birth wt. 1.8 kg. Mother received no prenatal care. Child approximately 6 wk. premature, delivered after a 3 hr. labor and vertex presentation, apparently in good condition when born. The infant received synkamin and was placed in an incubator with continuous oxygen, the oxygen being discontinued on the 10th day of life. Vitamin C was started on the 7th day, additional vitamin C and vitamins A and D on the 13th day. Temperature by the 14th day was fairly stable between 36.1° and 37.0° C. The patient received 20 cc. of plasma intravenously on the 16th day, was considered well enough to be out of the incubator on the 20th day. Iron therapy was started on the 25th day, child again receiving 20 cc. of plasma intravenously on the 26th day.

Type III (Totally irregular breathing): D. A. (see charts 14A-D), Negro baby girl, 5 days of age, wt. 1.9 kg. Birth wt. 1.9 kg. Mother's age 18 yr. Expected date of confinement not known. No siblings. The child's birth history revealed there was a premature rupture of membranes. Mother's Wassermann test was negative, blood pressure normal. Labor was 6½ hr.'s duration. No anesthesia was used. Type of delivery was not known. The child was said to have cried immediately upon birth. When received in the hospital at the age of ½ hr., the child was placed in an incubator with continuous oxygen. Synkamin 1 mg. was given daily for 3 days. The child was started on a gradually increasing standard formula for premature infants until, on the 5th day of life when record was taken, child was receiving 52 cal./lb. and 18 cal./oz. of formula. On the day the plethysmograph recording was made, the child's condition was noted to be very good. She had a sucking reflex, although she had been on continuous gavage feedings to that time. No vitamins had yet been given the baby.

The infant was quiet and asleep within a few minutes after being placed in the plethysmograph. Record of respirations was continuous; samples shown are representative, extracted from the continuous record.

Type IV (Regular breathing): S. M. (see charts 15 A-D), white baby boy. Birth wt. 1.3 kg. Aged 2 days. Wt. at 2 days was 1.2 kg. No prenatal history. Mother's serology was negative at 6 mo. of gestation. Cause of prematurity was unknown. This child was 1 of twins; the girl twin weighed 1.3 kg. and died at the age of 10½ hr. Labor was 7 to 8 hr.; both babies born of vertex

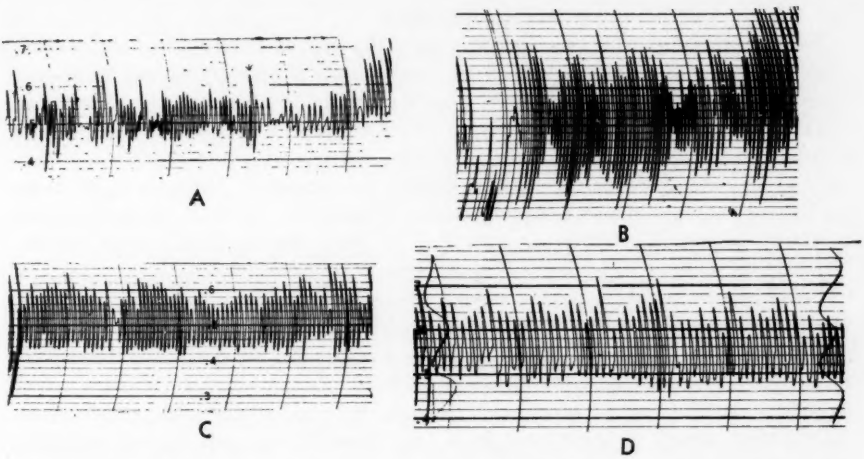


CHART 14 A. During 10th min., in room atmosphere, baby quiet and asleep. Respirations completely irregular, no periods of apnea noted. B. During 16th min., in 42% oxygen, note increased excursion, irregular respiration persisting. No periods of apnea noted. C. During 24th min., in 44% oxygen, respirations regular; no apneic periods. D. During 26th min., in 80% oxygen, respirations regular; no apneic periods.

presentation. There was no premedication except for a few whiffs of ether. Labor was said to be spontaneous. The child was said to have cried lustily at birth. The infant received continuous oxygen in an incubator, received synkamin intermuscularly after 1 day. Plethysmographic recording was made on the 2nd day of life. The baby at this time appeared very immature and premature. There was some edema of the face and hands. The skin was delicate and transparent, cranial bones easily compressible. Slight perioral cyanosis was noted when the child was out of oxygen. The child died 10 hr. after the plethysmographic recording was made.

The infant was quiet and asleep within a few minutes after being placed in the plethysmograph. Record of respirations was continuous; samples shown are representative, extracted from the continuous record.

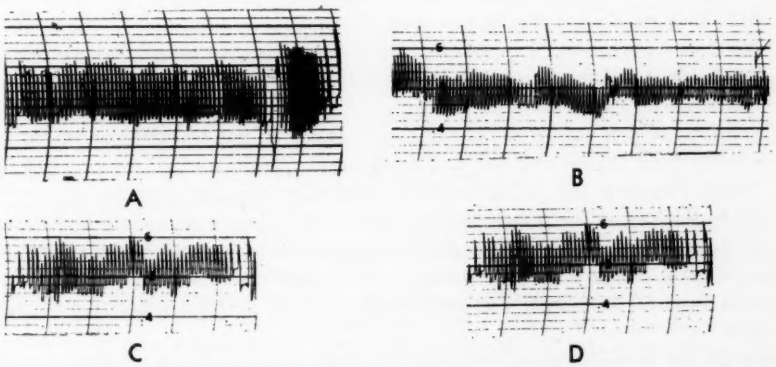


CHART 15 A. During 6th min., in atmosphere, respirations completely regular. B. During 10th min., in 34% oxygen, respirations remain regular. C. During 16th min.—in 64% oxygen, respirations regular. D. During 20th min., in 85% oxygen, respirations regular.

Discussion

Periodic breathing[16] has been described since the time of Hippocrates and has been observed in various conditions both in man and animals in both normal and pathologic states. It was noted some 40 years ago[17-18] that this type of breathing could be abolished in adults by the administration of pure oxygen. There are numerous explanations for periodic breathing, most of them based on the assumption that the respiratory center does not receive at all times a normal or constant stimulus to respiration. This in turn has been explained by changes in carbon dioxide tension of the blood,[19] anoxia,[20] changes in blood pressure,[20] excitation of chemoreceptors,[21] all of these causing possibly some primary depression of the medullary center and modification of motor impulses.[22]

Gesell stated[21] that the hypoxia occurring during apnea excites chemoreceptors to bring about augmented respiration. This increased pulmonary ventilation increasing carbon dioxide excretion and lowering blood and tissue levels so that the stimulus to the respiratory center is gradually reduced until apnea results.

Räihä and Salmi,[9] on the other hand, correlated the periodic respiration of premature infants with changes in blood hemoglobin level. However, our data (to be published) reveal that the premature infants studied when classified according to type of breathing, showed no correlation between type of breathing, hemoglobin level or age. That is, the babies with periodic respiration had as great a range of age and hemoglobin level as did those babies breathing with a regular type of respiration.

The exact mechanism of the periodic type of breathing or irregular breathing of these premature infants has not been ascertained nor the reason why oxygen acts as a stimulus to increase respiration and makes it more regular. Neither has it been generally agreed whether a greater or less than normal respiratory stimulus exists in these infants or whether they have a "mature" respiratory center.

It appears from the preceding data and from other reports presented from this laboratory[11, 23] that these infants have in atmosphere an arterial blood oxygen saturation which is within normal range for adults. Despite this, a high percentage of the infants breathed irregularly in atmosphere, but, as shown, responded to the administration of oxygen by breathing more regularly. Therefore, it would seem that these premature infants did have a reduced pulmonary ventilation in atmosphere inadequate to supply oxygen needs as evidenced by their response to the administration of oxygen.

From the data presented it appears that these infants have an oxygen lack and that the lack results from a defect in oxygen exchange from blood to tissues rather than from a lower hemoglobin saturation.

The carbon dioxide tension in most of these infants[11, 23] was essentially normal as compared to the adult control level and would indicate no "fault" in respiratory control from this factor. However, the periodic type of respiration suggests there are greater than normal fluctuations in the carbon dioxide tension which at present cannot be measured.

It remains to be proved that metabolic changes are effected by the administration of oxygen. Does it change a partially anaerobic metabolism to one which is wholly aerobic? Does the increased pulmonary ventilation result from an increased production of carbon dioxide?

Data has not yet been obtained regarding a change of carbon dioxide tension or production of organic acids during the administration of oxygen.*

* Although a number of determinations of arterial carbon dioxide content and pH were done while

Summary

Arterial blood studies were performed on 44 premature infants while in atmosphere and greater concentrations of oxygen. Analyses were made for oxygen content, oxygen capacity and hematocrit. Concomitant plethysmographic studies were made on 29 occasions. Results were as follows:

1. Only 25% (7) of the premature infants studied breathed regularly in atmosphere; the remaining individuals breathed with some degree of periodicity (44%) or completely irregularly (30%).

2. As the concentration of oxygen being breathed was raised, then more of the group shifted to a regular type of respiration until when in 75-85% oxygen, 88% of the group then breathed with a regular type of respiration.

3. a. The percentage arterial oxygen saturation of the group averaged 93% in atmosphere, 96% in 30-55% oxygen, 100% saturation in 70-79% oxygen being breathed and 102% in 80-89% oxygen.

b. In atmosphere, when compared on age basis, the younger group (1-14 days) had essentially the same arterial oxygen saturation as the older group (14-65 days). In an atmosphere of 70-90% oxygen, the saturation of the younger group increased to 102% while the older group rose to 100%.

c. When compared on body weight basis, the 0.9-1.3 kg. group increased the arterial oxygen saturation of 85% in atmosphere to 102% when 70-85% oxygen was administered; the 1.3-1.8 kg. group, 93% to 101%; the 1.8-2.3 kg. group, 9% to 100%. (It is noted that either on age or body weight basis the group with higher hematocrit attained higher arterial oxygen saturation when 70-85% oxygen was administered than the group with lower hematocrit.)

4. a. A statistical analysis of the respiratory records revealed an average rise of 30% in minute volume when 30-40% oxygen was administered, this rise being significantly maintained as higher concentrations (to 90%) of oxygen were administered.

b. An average significant rise in respiratory rate of 30% was noted when 30-40% oxygen was administered which slowly fell to the original rate level as oxygen administered was increased to 80-90% concentration.

c. Consequently, the tidal volume (volume per respiration) gradually increased to 30% above the level in atmosphere as oxygen administered was increased to 80-90% concentration.

Conclusion

The majority of premature infants breathe, while in air, as if suffering from oxygen lack, yet do not have a strikingly reduced arterial oxygen saturation. Nevertheless, the administration of oxygen corrects this type of breathing and causes a relative hyperpnea and increased pulmonary ventilation.

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these premature infants were in high concentrations of oxygen, it is not yet possible, because of insufficient data, to show any significant trend.

Moreover, even though the glass electrodes can be used in the presence of oxygen, calibration against the absolute pH standard, namely, hydrogen electrode, is naturally precluded due to the high oxygen content of these arterial blood samples. However, satisfactory determinations have been made on reduced blood with glass electrodes. Whether one can assume that the pH of arterial blood of subjects exposed to atmosphere with oxygen content as high as 75-80% can be determined with the glass electrode that has been calibrated with standard buffer solutions would be a problem for the physical chemists to settle.

Acknowledgments

The authors appreciate the cooperation of the medical and nursing staff of the Children's Hospital of Michigan and the Newborn Nursery staff of the Herman Keifer Hospital, Detroit, Dr. C. C. Craig of the Statistical Department of the University of Michigan, and Dr. F. D. Reardon, Jr., of the Pediatric Department, University of Michigan. Acknowledgment is particularly due Dr. Ann Lublin, Instructor in Pediatrics at Wayne University College of Medicine, who gave direct assistance in selection of patients and obtaining of samples.

Dr. Walter J. Nungester, Professor of Bacteriology, University of Michigan Medical School, granted the use of the recording galvanometer which greatly facilitated the study.

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SPANISH ABSTRACT

Respuesta Fisiológica y Química de Infantes Prematuros a la Atmósfera Enriquecida de Oxígeno

Se hicieron estudios de sangre arterial en 44 infantes prematuros mientras estaban en una atmósfera y concentraciones mayores de oxígeno. Se hicieron análisis para el contenido de oxígeno, capacidad de oxígeno y hematócrito. Concomitantemente se hicieron estudios pletismográficos en 29 casos. Los resultados fueron como sigue:

1.—Solamente 25% (7) de los infantes prematuros estudiados respiraban regularmente en la atmósfera; los individuos restantes respiraban con cierto grado de periodicidad (44%) o con completa irregularidad (30%).

2.—A medida que la concentración de oxígeno que se estaba respirando era aumentada, entonces más infantes en el grupo cambiaban a un tipo regular de respiración hasta que, cuando en 75-85% de oxígeno, 88% del grupo respiró con un tipo de respiración regular.

3.—a. El porcentaje de saturación de oxígeno arterial del grupo tuvo un promedio de 93% en atmósfera, 96% en 30-55% de oxígeno, 100% de saturación en 70-79% de oxígeno que se estaba respirando y 102% en 80-89% de oxígeno.

b. En atmósfera, cuando se compara a base de edad, el grupo menor (1-14 días) tenía esencialmente la misma saturación de grupo arterial que el grupo mayor (14-65 días). En una atmósfera de 70-90% de oxígeno, la saturación del grupo menor aumentó a 102% mientras que el grupo mayor subió a 100%.

c. Cuanda se compara a base de peso de cuerpo, el grupo de 0.9-1.3 Kg. aumentó la saturación de oxígeno arterial de 85% en atmósfera a 102% cuando 70-85% de oxígeno fué administrado; el grupo de 1.3-1.8 Kg. 9% a 100%.

(Se ha notado que ya sea a base de edad o de peso de cuerpo, el grupo con hematócrito alcanzó mayor saturación de oxígeno arterial cuando se administró 70-85% de oxígeno que el grupo con hematócrito bajo).

4.—a. Un análisis estadístico de los records respiratorios reveló un alza media del 30% en volumen de minuto cuando se administró 30-40% de oxígeno, esta alza es significativa pues concentraciones más altas (a 90%) de oxígeno fueron administradas.

b. Se notó un alza media significativa en la proporción respiratoria del 30% cuando se administró 30-40%, la que bajó lentamente a cantidad de la proporción original a medida que la concentración aumentaba a 80-90%.

c. Consecuentemente, el volumen periódico (volumen por respiración) aumentó gradualmente a 30% arriba del nivel en atmósfera a medida que el oxígeno administrado aumentaba a 80-90% de concentración.

University of Michigan

DOES GLUTAMIC ACID ADMINISTRATION INFLUENCE MENTAL FUNCTION?

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Oakland and Berkeley, Calif.

DURING the past five years considerable interest has been stimulated in the possible beneficial effects of glutamic acid in improving mental function, particularly among retarded individuals. Price, Waelsch and Putnam,[1] in a study of epilepsy, reported an increased mental and physical alertness in patients treated with dl-glutamic acid hydrochloride. This prompted further study (Albert et al.[2]) on the effect of free glutamic acid in mentally retarded subjects, and the results of this investigation appeared to support the earlier observation that glutamic acid improves mental function. Both studies dealt with groups of eight and the data were presented in the form of case histories. Three additional reports by Zimmerman, Burgemeister and Putnam[3–5] have appeared more recently. Their first paper[3] was a preliminary study based on nine cases. Taking cognizance of the smallness of the group, they regarded their results as tentative but remarked (p. 13) that ". . . the consistent improvement reflected in the psychological test scores under the conditions of our experiment suggests that glutamic acid may have a genuine facilitating effect on mental functioning in human subjects, as it does on maze learning in the white rat." In the second report,[4] 69 patients were studied, of which 28 were subject to convulsive disorder (11 being mentally retarded as well), and 33 were mentally retarded without convulsive manifestations. The paper summarized psychometric results after six months of therapy in which glutamic acid was administered in doses up to 24 gm. daily. The authors concluded from a statistical analysis of their data that glutamic acid accelerates mental functioning in a general way (as indicated by verbal, motor and Rorschach tests), that results are most striking in seriously retarded individuals, and that greater improvement occurs in processes involving abstract thought than in motor skill. The third paper[5] presented findings for the first 30 cases in the group described to complete a year of glutamic acid therapy. It consisted of 16 with mental retardation, 7 with convulsive disorder as well and 7 with convulsive disturbances alone. The authors concluded that acceleration of mental function during the second six month period was not as great as that observed in the first six month period, and that the rate of improvement appeared to be approaching a limiting value.

Prior to publication of these last three reports, the present investigators became interested in the problem since it offered a possibility of accelerating the rehabilitation of individuals afflicted with spastic paralysis and other forms of neuromuscular disorder with which they were concerned.

EXPERIMENTAL

Selection of Cases: The present study is based upon findings for 33 feebleminded patients at the Sonoma State Home in Eldridge, Calif. They were selected primarily on the basis of unequivocal

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diagnosis of primary or secondary feeblemindedness, without epilepsy or other neurologic involvement. Since preliminary examination of the data revealed no significant differences between cases of primary and secondary feeblemindedness, the 2 diagnostic categories were combined for purposes of this investigation. Insofar as possible, adolescent subjects were selected in preference to other age groups, the majority of cases falling between 10 and 17 yr. of age.

Experimental Design: Cases selected for inclusion in the study were divided into experimental and control groups approximately equated on the basis of Stanford-Binet I.Q. (taken from patients' charts), sex, age and type of feeblemindedness. All subjects were then examined with a battery of psychologic tests. Originally 40 cases were selected and divided into 20 matched pairs on the basis of the criteria previously mentioned. Such individual matching is necessarily only approximate. Further, in the present instance 7 cases had to be omitted from the final evaluation for various causes unrelated to the experiment; e.g., sickness, transfer, etc. For this reason the analysis is based upon comparison between experimental and control groups, rather than between paired individuals. However, the allocation of cases to the experimental or control group on the basis of matched pairings aided in equating the groups with respect to the criteria. As may be seen from table 1, the 2 groups are very similar. In the control group there were 10 males and 5 females; in the experimental group, 12 males and 6 females. Average age for the control group was 13 yr., 9 mo.; for the experimental group, 15 yr., 2 mo. There were 4 cases of primary feeblemindedness and 11 of the secondary type in the control group; there were 5 primary and 13 secondary in the experimental group. The mean pretreatment performance of the control group (see table 2) was by no means identical with that of the experimental group but the method of statistical analysis utilized makes appropriate allowance for the initial differences between groups in evaluating their relative gains. It is interesting, however, that pretreatment mean M.A.'s on the Stanford-Binet are extremely close, 77.4 mo. for the control group and 76.8 for the experimental, despite the fact that the assignment of cases to 1 group or the other was based on an earlier Stanford-Binet I.Q. recorded on each patient's institution chart.

There followed a treatment period of 17 wk. during which the experimental group received glutamate and the control group a placebo. A lapse of about 4 mo. between the pretreatment psychometric appraisals and the commencement of glutamate administration brings the total test-retest interval to approximately 10 mo. During this 4 mo. period the environment was not altered in any significant way. Throughout the entire period of the investigation experimental and control cases were patients in the same institution, on the same regimen and receiving the same care and diet, the latter being prepared in a central kitchen. At fortnightly intervals during the treatment period the patients were examined and the aides who administered the preparations were interviewed. At the conclusion of this period, all cases were re-examined with the same psychometric battery given before the treatment. Fasting blood specimens and 24 hr. urine specimens were collected at the end of the experimental period. The glutamic acid and glutamine content of plasma, and the glutamic acid content of urine, were determined. These data will be published elsewhere. The influence of glutamate was evaluated in terms of the change from pretreatment to post-treatment test status of the experimental group, as compared with the control. The statistical procedure used for this evaluation was the method of co-variance as described by McNemar.[6]

Administration of Monosodium Glutamate: Instead of free glutamic acid, the subjects received the monosodium salt of 1(+) glutamic acid (called MSG in this report), prepared in a highly purified form.* Since the salt is very soluble, it was possible to prepare a 44.3% solution (40% as the anhydrous form), made up with distilled water and flavored with a minute quantity of peppermint oil (peppermint water 5 ml./l. solution). This was given to the experimental group in equal doses 3 times daily, postprandially. Control subjects received the placebo—distilled water flavored with peppermint water (5 ml./l.). The solutions were labeled A. (for placebo) and B. (for MSG), and the hospital aides who administered them were led to believe that both preparations might be beneficial. Both solutions were administered in the same manner, as follows: all subjects were started with 10 ml. doses on the 1st day. The dose was raised to 15 ml. on the 2nd day and this dose was maintained for 1 wk.; i.e., MSG 18 gm./experimental subject/day. At this time the dosage was increased to 20 ml. for all subjects (MSG 24 gm./day), and maintained for the subsequent 16 wk. The solutions were introduced into the posterior portion of the mouth by means of a syringe. This was followed by a half

* This material was provided by the International Minerals and Chemical Corp., Chicago.

glass of water. Careful dosage records were kept and only rarely was a dose omitted. The MSG solution was mildly unpleasant in the concentrations used but no serious untoward reactions were observed.

Psychological Tests: The Standard-Binet Form L (1937 revision) was administered at the beginning of the experiment, and Form M was given at the end of the experimental period. The following tests completed the battery: Cornell Coxe Performance Ability Scale; Porteus Maze; Thurstone and Thurstone Primary Mental Abilities, Ages 5 and 6, and the Rorschach Test. All the testing was performed by 2 psychologists who worked as a team.

Results

The psychometric data are presented in table 1. For purposes of analysis raw scores were employed

TABLE 1*

Case No.	Age (yr.-mo.)	Sex	Stanford-Binet (mo.—ment. age)		Cornell Coxe (wt'd score)		Porteus Maze (mo.—ment. age)		Thurstone (point score)		Thurstone (Motor) (point score)	
			Before	After	Before	After	Before	After	Before	After	Before	After
						Control						
1	21–6	M	82	78	—	—	—	—	100	98	25	24
2	18–2	F	90	108	122	155	72	96	108	111	35	34
3	15–4	M	110	100	134	173	126	132	110	117	18	30
4†	15–3	F	84	90	205	221	162	186	122	119	—	—
5†	15–2	F	86	96	191	201	114	108	100	114	37	44
6	15–0	M	140	116	167	211	144	144	120	120	29	36
7	15–0	M	76	90	98	138	114	144	87	100	35	46
8	14–5	F	110	106	54	89	66	60	100	94	21	27
9	14–3	F	42	37	—	—	—	—	—	—	—	—
10†	14–2	M	82	102	172	198	150	186	112	108	33	44
11	12–6	M	—	—	61	128	48	72	38	49	10	20
12	11–10	M	37	46	—	—	—	—	—	—	—	—
13	10–1	M	70	69	—	—	—	—	31	37	—	—
14	7–2	M	43	44	—	—	—	—	—	—	—	—
15†	6–2	M	32	39	—	—	—	—	—	—	—	—
						Experimental						
16†	29–4	M	86	88	205	225	174	192	104	116	34	34
17	25–6	F	106	108	109	120	90	132	82	88	5	2
18	24–7	M	180	188	—	—	180	198	119	124	34	44
19	19–9	M	114	96	154	168	114	150	101	105	14	26
20	17–3	M	112	116	210	285	168	186	115	115	57	48
21	16–10	M	70	68	99	76	48	60	53	89	20	29
22	16–9	M	68	59	—	—	36	48	31	38	10	12
23	16–0	F	78	72	50	84	—	—	80	84	25	6
24†	14–2	M	78	92	124	147	72	90	99	107	31	46
25†	12–10	F	84	104	198	205	192	186	108	109	28	55
26	12–5	M	50	54	—	—	—	—	27	32	21	15
27	12–5	F	68	55	—	—	—	—	—	—	—	—
28	10–10	M	59	66	56	74	54	66	43	57	25	32
29	10–4	F	76	74	78	96	60	60	49	65	37	39
30	9–8	M	53	61	—	—	72	48	—	—	—	—
31	9–4	F	27	33	—	—	—	—	—	—	—	—
32†	8–1	M	45	47	—	—	42	48	—	—	—	—
33†	6–2	M	29	30	—	—	—	—	—	—	—	—

* Owing to the level of difficulty of the tests used and to various circumstances beyond control (e.g., illness or uncooperativeness of subjects), it was not possible to secure scores for all cases on all tests.

† Primary feeblemindedness Control —15 cases, total ave. age 13 yr., 9 mo.;
Experimental—18 cases, total ave. age 15 yr., 2 mo.

throughout; i.e., months of mental age for the Stanford-Binet and Porteus Maze; total weighted score for the Cornell Coxe; and total point score for the Thurstone and Thurstone. Since, in the latter, the Motor test is treated separately from the 4 other components of the test, it is also presented separately in table 1. Table 2 gives the F-ratios obtained by analysis of co-variance, along with the mean values

TABLE 2

	Control						Experimental						
	No. of Cases	Mean Before	Mean After	Gain	After Adj.	Adj.* Gain	No. of Cases	Mean Before	Mean After	Gain	After Adj.	Adj. Gain	F-Ratio
Stanford-Binet	14	77.4	80.1	2.7	79.8	2.4	18	76.8	78.4	1.6	78.6	1.8	.09
Cornell Coxe	9	133.8	168.2	34.4	165.4	31.6	10	128.3	148.0	19.7	150.5	22.2	2.21
Porteus Maze	9	110.7	125.3	14.6	118.9	8.2	13	100.2	112.6	12.4	117.1	16.9	.06
Thurstone (total)	11	93.5	97.0	3.5	89.5	−4.0	13	77.8	86.9	9.1	93.2	15.4	1.30
Thurstone (motor)	9	27.0	33.9	6.9	33.5	6.5	13	26.2	29.9	3.7	30.1	3.9	.62

* Adjusted gain.

before the period of treatment, and the adjusted and unadjusted mean values after treatment. Since the smallest F value required to demonstrate significance at the 5% level of confidence for 29 degrees of freedom, as in the Stanford-Binet sample, is 4.18 it is clear that none of the psychologic tests employed under the conditions of this study demonstrate, statistically, a beneficial effect of MSG upon the intelligence or performance ability of feebleminded individuals.

The Rorschach tests were graded in terms of Form Level. Customary statistical analysis and computation of "t" gave a very low value for the latter. Owing, however, to the lack of general agreement among experts on the criteria for rating form level (Beck,[7] Klopfer and Kelley[8]), the Rorschach data have been omitted from the main statistical analysis.

Subjectively, no significant impressions were reported by any of the individuals concerned with the study. Occasional comments that a particular subject seemed to show improvement proved to fall more or less equally among both control and experimental subjects.

Discussion

How may one account for the negative findings of the present investigation in the light of the positive reports of Zimmerman et al.? In this study the neutral monosodium salt of glutamic acid was administered rather than the free acid. In terms of the dosage given, the added sodium would be equivalent to nearly 1 gm. for each dose or, expressed as sodium chloride, 2.5 gm. It is difficult to see how such quantities of sodium could seriously alter the physiologic situation. Moreover, if glutamic acid plays some unique role in nerve metabolism, as is evident from the studies of Weil-Malherbe[9] and Nachmansohn et al.,[10] it is even more unlikely that such quantities of sodium could nullify the effect in the human organism.

Careful examination of the reports of Zimmerman et al. suggests that differences in degree of experimental control, in the design of the investigation, and in the nature of the statistical analysis may account for differences between their findings and those of the present study. They comment[5] on the difficulty of getting parents to administer glutamic acid faithfully, suggesting that the cases were living in their own homes and susceptible to many influences besides that of glutamic acid (including parental belief in the value of the treatment) which might have affected the mental stimulation they received and, indirectly, their test performance. In contrast, subjects of the present study were living in a more nearly controlled environment with the same diet, regimen, etc., throughout the investigation.

A major difference between the design of Zimmerman et al. and the present research lies in the nature of the groups used as controls. Their control group consisted of 37 cases who had been tested from six months to eight years previously, and who were incorporated into the experimental group and retested both before and after glutamic acid

therapy. Comparisons were then drawn between control gains over long intervals varying from case to case, and experimental gains over the relatively brief period of glutamic acid treatment. In contrast, the interval between testings in the present study was the same for all cases in both control and experimental groups, which would seem to be a much more satisfactory experimental design. This difference in the two studies is especially significant in relation to practice effect. If practice effects are important in determining test score, but tend to "wear off" after an interval, retests after a short time will show a gain, while retests over long intervals will be relatively unaffected. Since in the Zimmerman study[4] the control test-interval averaged 2 years, 11 months, while the experimental test-interval was only 6 months, the finding of a gain only during the latter period is compatible with the hypothesis that the improvement attributed to glutamic acid may, in fact, be due to practice. The discovery of a "ceiling effect" in the second 6 month interval (1948) is likewise consonant with the well known finding that successive increments of practice produce diminishing returns in psychometric performance. That Zimmerman et al. may have underestimated the influence of practice, at least insofar as the Grace Arthur Test is concerned, is suggested by the findings of Patterson.[11] Using the Grace Arthur Scale, he demonstrated that a group of mentally deficient children progressed at the rate of normal children, i.e., an advance of 12 performance age months per year, when given the practice afforded by yearly re-examinations.

A further point of difference between the studies of Zimmerman et al. and the present one lies in the method of data analysis. Many of their comparisons are expressed in units of I.Q. However, the chronologic age (C.A.) range of their subjects is such that for some cases I.Q.'s must have been based on actual C.A.'s; for other, the I.Q.'s must have been based on the arbitrary C.A. of 15 used for people of 16 years or older, or on the semi-arbitrary C.A.'s used in the age range from 13 to 16. This source of variation may have biased their comparisons, especially if the method of calculating the test C.A. changed for any cases during the course of the experiment. Further, there is no general agreement as to the applicability to feebleminded individuals of the findings concerning the curve of normal mental growth upon which the use of an arbitrary C.A. depends. In view of these considerations it seemed preferable to the present authors to use raw scores instead of ratios to express test status, on the assumption that any genuine improvement in a subject would be manifested in a larger number of items being performed correctly on the test in question.

For the foregoing reasons, and from the evidence adduced above, it is concluded that a beneficial effect of glutamic acid in the treatment of feeblemindedness has not been demonstrated.

Summary

Thirty-three feebleminded individuals, mostly adolescents and without epilepsy or other neurologic involvement, were divided into two groups well matched as to intelligence quotient, sex, age and type of feeblemindedness. One group received orally 1(+) monosodium glutamate, 24 gm. daily, for 17 wk. The other group served as controls and received a placebo given at the same time and in like manner. Throughout the entire period of the investigation, experimental and control cases were patients in the same institution, on the same regimen and receiving the same care and diet, the latter being prepared in a central kitchen.

The following psychologic tests were administered before and after the experimental period: Stanford-Binet (Form L before and Form M after), Cornell-Coxe Performance

Ability Scale, Porteus Maze, Thurstone and Thurstone Primary Mental Abilities and the Rorschach Test.

On the basis of detailed statistical analysis employing the method of co-variance, no significant difference between control and experimental subjects could be shown, and it was therefore concluded that a beneficial effect of glutamic acid in the treatment of feeblemindedness has not been demonstrated.

Acknowledgment

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Spanish Abstract

Tiene el Acido Glutámico Influencia Sobre la Función Mental?

Treinta y tres individuos imbéciles, la mayor parte adolescientes y sin epilepsia u otra afección neurológica, fueron divididos en dos grupos bien igualados en cuanto a cosiente de inteligencia, sexo, edad y tipo de imbecilidad. Los pacientes en un grupo recibieron oralmente 24 gm. diarios de 1 (+) glutamato de monosodio por 17 semanas. Los pacientes en el otro grupo sirvieron como control y recibieron un placebo dado al mismo tiempo en una meanera similar. Durante todo el período de investigación, los pacientes de experimentación y de control permanecieron en la misma institución, en el mismo régimen y recibieron el mismo cuidado y dieta, habiendo sido la última preparada en la cocina central.

Los siguientes ensayos psicológicos fueron administrados antes y después del período experimental: Stanford-Binet (Forma L antes y Forma M después), Escala de habilidad Cornell-Coxe, Porteus Maze, habilidades mentales primarias Thurstone y Thurstone y Rorschach.

A base de análisis estadísticos detallados empleando el método de co-variación no se pudo demostrar diferencia significativa entre sujetos de control y de experimentación, así es pues que se llegó a la conclusión de que un efecto benéfico del ácido glutámico en el tratamiento de imbecilidad no ha sido demostrado.

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POSTINFANTILE CORTICAL HYPEROSTOSIS WITH SUBDURAL HEMATOMA

Report of Case and Review of the Literature

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INFANTILE cortical hyperostosis has been a recognized clinical entity since it was described by Caffey and Silverman[1] in 1945; but a coincident subdural hematoma has not previously been recorded. Such a coincidence was recently observed in a child with postinfantile cortical hyperostosis and is of special interest because of the relative frequency of both conditions after early infancy. This case will be described and the 32 previously reported examples[1-15] of infantile and postinfantile cortical hyperostosis will be discussed.

REPORT OF CASE

C. McG., a white girl 29 mo. old, had had pain in the shoulder for 4 wk., a limp due to painful feet for 2 wk., and enlargement of the head for 3 days, together with coarseness and loss of hair. One of the first symptoms noted was irritability whenever she was handled about the arms. Slight limp developed during the next 2 wk. and the feet became swollen, tender and painful. RG of the right clavicle taken 1 wk. prior to admission revealed an adjacent soft tissue swelling in the middle third. In the next few days the entire chest seemed tender and she could not turn over in bed. Three days before admission increased irritability, photophobia and extreme lassitude were noted and for the first time she had fever of 38.2° C. The mother then noted bilateral swelling about the upper part of the face associated with constant pain in the ears. The possibility of trauma was denied by the parents.

The child had been delivered by breech after an uneventful pregnancy. Birth weight was 3.7 kg. Neonatal course and development was normal. Since 11 mo. of age, she had had frequent sore throats with fever; the last of these occurred about 2 wk. before the present illness. Vitamin C intake consisted of orange juice fortified with ascorbic acid (25 mg. daily) begun at the age of 2 wk. A proprietary vitamin concentrate furnishing vitamin A natural fish oil 60,000 I.U. and vitamin D 8,500 I.U./gm. was given in daily doses of 10 drops, from 2 wk. until 1 yr. of age. Then, the dosage was increased to 30 drops (approximately 37,500 I.U. of vitamin A) daily; it had been maintained at that level until admission.

On admission, the patient weighed 13.6 kg. and was 93 cm. tall. Temperature was 38.2° C.; pulse 136/min.; respiration 22/min.; blood pressure 120/80 mm.Hg. Hyperirritability was extreme; mild photophobia, pseudoparesis of right arm and seborrheic plaques over right shoulder and thighs were noted. Hair was dry and coarse but there was no alopecia. Both fontanelles were closed and Macewen's sign was positive. Symmetric and bilateral soft tissue swelling was present from the orbital ridge of the zygoma extending posteriorly to the temporomandibular junction; this did not pit on pressure. Tympanic membranes and fundi were normal. Movement of right arm caused pain and there was obvious tenderness over the prominent right clavicle. Both feet were tender and swollen; she refused to walk and was reluctant to move her legs. Tendon reflexes were symmetrically active.

Hemogram: WBC count 12.44 thousand (53% lymphocytes, 45% leucocytes and 2% monocytes). Hgb. 8.9 gm./100 cc. and RBC count 3.3 million. Erythrocytic sedimentation rate 61 mm. in 1st hr. (Westergren, uncorrected). Bleeding time 5 min., 45 sec.; clotting time 3 min., 39 sec. Platelets 197 thousand/cmm. and prothrombin activity 82.5% of normal. Serologic reaction for syphilis and

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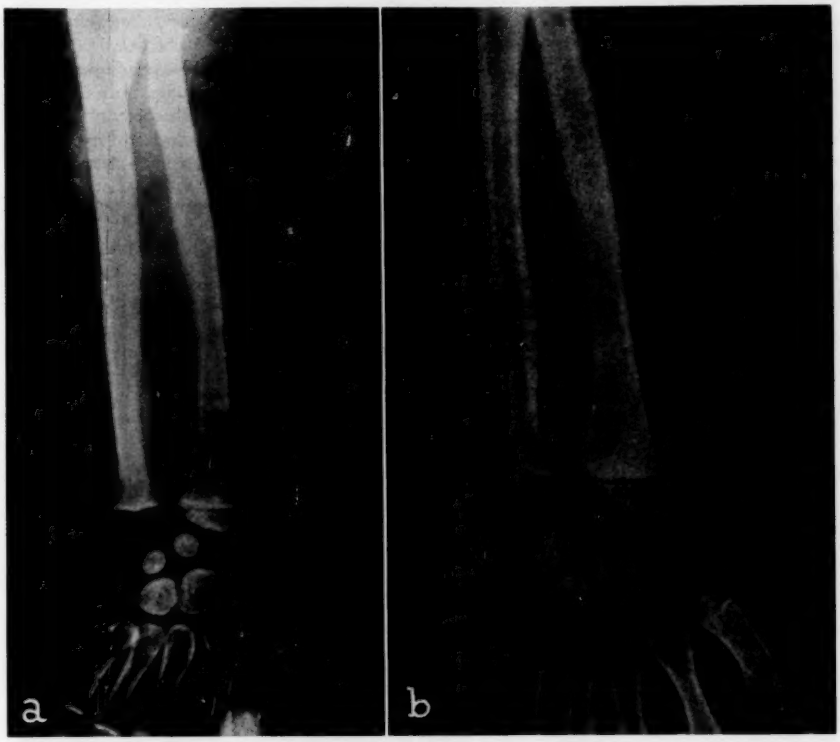

FIG. 1. Roentgenograms of right ulna showing: (a) subperiosteal thickenings with periosteal elevations, 3 wk. after onset of symptoms; (b) evidence of resolution and calcification of lesion, 12 wk. after onset.

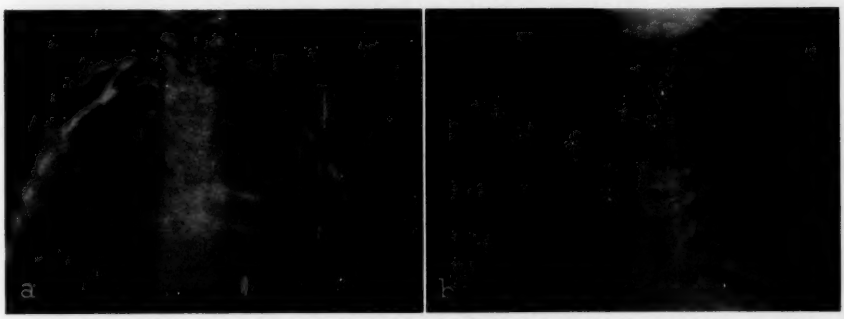

FIG. 2. Roentgenograms of clavicles showing: (a) similar areas of fusiform calcification, 3 wk. after onset; (b) evidence of resolution and calcification of lesion, 12 wk. after onset.

Mantoux and histoplasmin skin test reactions were negative. Serum calcium was 4.4 and phosphorus, 1.17 in mEq./1. Serum alkaline phosphatase was 15.4 Bodansky u. Three blood cultures remained sterile and results of repeated cultures from the throat were considered noncontributory.

RGs of the skull were interpreted as showing definite enlargement in the posterior fossa and a scaphocephalic contour. There were no evidences of increased intracranial pressure or calcification. The temporomandibular joint appeared normal. Skeletal age coincided with the chronologic age. Along the distal portion of the right ulna was a zone of periosteal thickening which "could have been the result of an old greenstick fracture" (Fig. 1a). Similar areas of fusiform calcification were

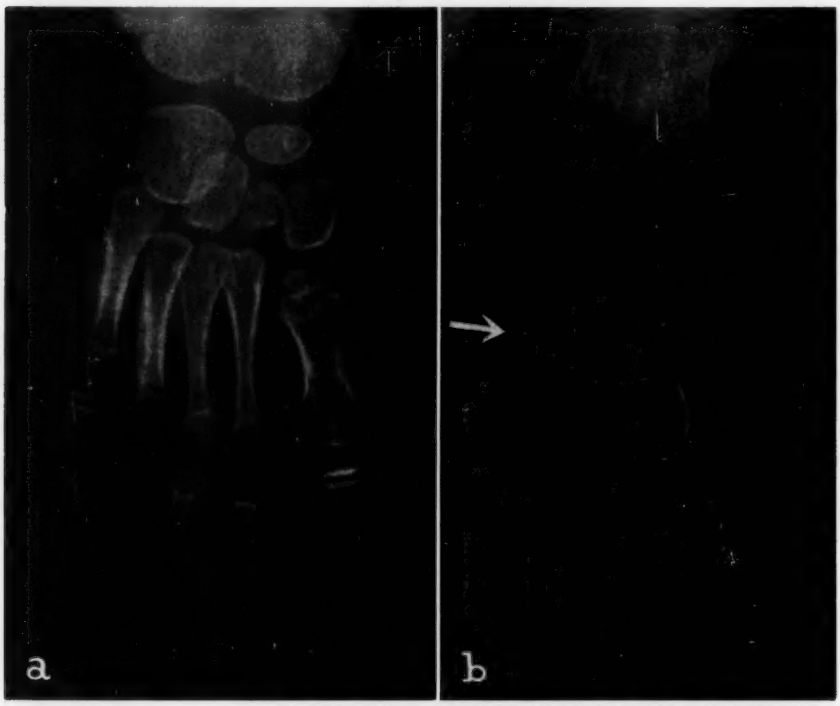

FIG. 3. Roentgenograms of left 5th metatarsal showing: (a) similar areas of fusiform calcification, 3 wk. after onset; (b) evidence of resolution and calcification of lesion, 12 wk. after onset.

observed along both clavicles (Fig. 2a), the inferior margin of the right 7th rib and the shaft of the left 5th metatarsal (Fig. 3a).

Penicillin and sulfadiazine were given in conventional dosages without apparent effect. The low grade fever gradually subsided within 6 days and there were only 2 transient febrile periods thereafter; blood cultures were sterile on both of these occasions. Liquid antihistaminic preparations were given for the symptomatic relief of itching associated with seborrhea. Following 2 blood transfusions of 250 cc. each, the RBC count rose to 4.48 million and Hgb. to 82%. One week after admission ESR was 77 mm. in 1 hr.

Because of the extreme irritability and positive Macewen's sign, a neurosurgical consultation was requested. Hydrocephalus was suspected and the day after admission, bilateral temporoparietal trephination was performed. Left trephination disclosed a normal but slightly tense and pulsating dura; 45 cc. of clear colorless fluid was obtained from the lateral ventricle. Right trephination revealed bluish discoloration of the underlying dura. There was nothing to indicate that extradural bleeding had

occurred. Through a nick in the dura a pulsating, thinly encapsulated blood clot was seen and successfully evacuated by suction, and partial removal of the hematoma-membrane was accomplished. At this point the thickness of the membrane did not exceed 3 mm. Exploration did not reveal any tear of the meninges. Chemical, cytologic and bacteriologic examination of the left ventricular fluid disclosed no abnormalities.

On the 3rd postoperative day, there was a definite, gradual change in personality from an irritable, sullen and resentful child to one who was happy, playful and contented. She accepted a varied diet, with specific supplements of vitamin D, 800 I. U., together with 4 to 6 ounces of orange juice daily. Within 2 wk. all symptoms and signs noted on admission had subsided except for equivocal tenderness over the right clavicle and questionable disinclination to walk.

After 4 wk. at home the mother reported there was still some pain about the feet. Examination confirmed these observations. Sedimentation rate was still elevated—74 mm./hr. During the next 8 wk. there was occasional discomfort in the feet.

When readmitted 12 wk. later for revision of the right trephination scar, the patient appeared well nourished and developed and was playful. She had gained 0.9 kg. Examination showed no abnormality except superficial cutaneous infection about the site of the right trephination scar and a small, nontender, fusiform swelling along the lateral border of the left 5th metatarsal. Hemogram yielded normal results and the ESR was 10 mm./hr. RGs of the forearm (Fig. 1b), clavicles and ribs (Fig. 2b) and the feet (Fig. 3b) revealed pronounced resolution and calcification of the original periosteal lesions. The contour of the skull was unchanged. Debridement of the right trephine was completed and the child was discharged 5 days later.

Eight and one half months after onset of the illness the trephine incisions were well healed; RGs of the clavicles were normal as was the ESR. All abnormalities present on admission—painful extremities, pseudoparalysis of the right arm, irritability, photophobia, facial swelling, dry coarse hair, seborrheic plaques and fever—had disappeared within 4 mo. of the onset.

Comment

The coexistence of cortical hyperostosis and subdural hematoma in this patient recalled a similar association previously noted by Caffey,[16] when he discussed periosteal contusions with or without visible fractures in a group of six infants suffering from chronic subdural hematoma. In the present case, the hyperostotic lesions were apparently of the postinfantile type thought to be associated with hypervitaminosis A.[17, 18] Clinical lesions associated with large doses of vitamin A have been noted by Toomey and Morissitte,[13] Dickey and Bradley,[14] Rothman and Leon[15] and Josephs.[19]

The subdural hematoma or traumatic episode could not be recalled that might have caused widely scattered periosteal contusions. Although the evidence for production of cortical hyperostosis due to vitamin A poisoning seems adequate, the pathogenesis of these associated lesions is not clear.

The causal mechanism in the early infantile group of cortical hyperostosis, although uncertain, has been likened to that observed in traumatic ossifying periostitis as described by Snedecor and associates;[20] however, Burke and Ross[9] considered such a theory untenable. There is no basis for supposing a deficiency of vitamin C in the case described in this paper or in many others.[1, 3, 5, 7, 9]

Interest in the coexistence of subdural hematoma with cortical hyperostosis of the postinfantile type was heightened when the relationship of the latter lesion to large doses of vitamin A was pointed out by Caffey.[17] In three of five examples of hypervitaminosis A previously reported in some detail,[13, 15, 19] with or without cortical hyperostosis, hemorrhagic manifestations have made up part of the clinical pictures. Other causes for hemorrhage were not clearly elucidated in these patients. It seems logical to believe that the two lesions observed in this patient might have had a common etiologic basis—perhaps vita-

min A. The fact that the daily dose of vitamin A, although excessive, was smaller than that recorded for previous examples, suggests that if this etiologic relationship can be proved then the minimal toxic dose may be smaller than previously suspected. So far as could be determined, hemorrhagic manifestations have not been described in experimental work dealing with toxicity of vitamin A. This report indicates a need for exploring such a relationship further.

Incidence

Although the majority of reports on infantile cortical hyperostosis have originated in the United States, the occurrence is not so limited.[10,11] That it is not uncommon is reflected by the number of cases reported since 1945. It is possible that such instances were observed earlier by Meier[21] and Chiari[22] but they were not generally recognized as clinical entities until Caffey and Silverman's description 10 years later.

Two thirds of the reported examples of infantile cortical hyperostosis have occurred in males. Evidence of the syndrome appeared before the fifth month of life in 24 of the 32 cases; onset in the remaining patients, 4 (50%) of whom had recognizably large doses of vitamin A, was between 14 and 36 months. In the case described in this paper the patient was 29 months old.

Etiology

As might be expected with discovery of any new syndrome, many causes must be considered and to date no single one has been definitely proved. The possibility of a hereditary factor is suggested by a recent report of van Zeben,[10] who described three patients with this condition in one family, each having typical periosteal lesions. No mention is made of environmental or dietary factors which may have been related. One, a boy 2 months old, later died at 6 months of age of complicating mastoiditis. No autopsy was performed. An older child of these parents had manifested typical features of cortical hyperostosis at 6 weeks of age; recovery, except for forward curvature of the tibia, was uneventful. The other member of the family with the disease was a boy 3½ months old, a second cousin.

Atypical infections, either bacterial, viral or rickettsial, must be considered. However, in none of 10 cases in which biopsy was performed was a typical picture of infection described. Antecedent infection of the upper respiratory tract in 20% of the reported cases[1,2,8] deserves mention. Further study is necessary to establish its significance. Trauma to involved areas might be suspected but has been repeatedly denied.[16]

Recently, hypervitaminosis A has been suggested as an etiologic possibility in postinfantile forms of the syndrome.[17,18] Dramatic improvement has been noted in a few patients after the administration of excessive doses of vitamin A was discontinued.

Bony lesions in younger and older age groups are radiologically similar. However, involvement of the mandible has not been reported in the older age group, whereas lesions affecting the bones of the feet are perhaps more common. The minimal dosage of vitamin A in postinfantile cortical hyperostosis necessary to produce the lesions has not been reported. The growing practice of prescribing highly potent vitamin preparations may result in prolongation of effects, related to larger hepatic stores of vitamin A.[23]

An allergic phenomenon with subperiosteal edema and adjacent soft tissue swelling has been discussed by Caffey and Silverman[1] and Shuman.[8] The latter tried various antihistaminic preparations, large doses of vitamin C and elimination diets to no avail; he

concluded that if this disease had an allergic background, it remained refractory to current antiallergic therapy.

Another etiologic possibility is a blood-clotting deficiency capable of producing subperiosteal hemorrhage and oozing from small blood vessels beneath the dura. Laboratory indices as to blood clotting were considered normal in the present case. Future cases will offer an opportunity to study these more closely.

Pathology

There have been no reports of postmortem studies. Biopsies in 10 reported cases[1-4, 6, 9, 12, 13] have shown periosteal hyperplasia with inflammatory infiltration. Burke and Ross[9] stated that their specimen obtained by biopsy did not reveal evidences of infection; cultures remained sterile and attempts to demonstrate a viral agent failed. Many osteoblasts infiltrating the cell cords of the marrow were noted in the specimen from van Zeben's 6 weeks' old patient.[10] Dickson and associates[4] described inflammatory changes of edematous muscle overlying a scapular lesion. A proliferating cartilaginous line with cells in clumps and new periosteal bone formation in the cortex without evidence of preceding hemorrhage was described by Smyth and associates,[2] who also noted fibrosing osteitis accompanying muscular dystrophy in one case.

Clinical Manifestations

Hyperirritability, fever (38.2° to 40.5°C.) and anemia with leucocytosis have been outstanding clinical features of most of the cases thus far reported. Invariably associated with these manifestations and the chief complaint are tender and painful bony swellings, frequently accompanied by overlying soft tissue tumefactions. Generally the appetite is adequate; in some it has been diminished. Nutrition is usually fair, although some patients may have a temporary retardation in weight gain.

In the youngest infants tender swellings arise suddenly without redness, discoloration or localized heat. Mandibular swellings are prominent and common, but involvement of the bones of the feet is unusual. The mandibular swelling is typically brawny, tender and nonerythematous, and does not pit on pressure. No particular cause has been suggested. Pronounced generalized lymphadenopathy was recently observed by O'Reilly[11] in a boy 2 months old with the characteristic radiologic findings. Such enlargement persisted for approximately three months, then gradually subsided.

Laboratory Studies

Anemia of mild degree, hypochromia, leucocytosis with a predominance of lymphocytes and an elevated erythrocytic sedimentation rate were noted in practically all the reported cases. Febrile agglutination titres, serologic tests for syphilis, tuberculin tests and blood levels of vitamin C have not been helpful in a positive sense. An increase in pressure of cerebrospinal fluid was observed by Kane and Borzell[6] and Delano and Butler[7] while in Whipple's case[5] it was reported to be normal.

Concentrations of calcium and phosphorus in blood sera have been normal. A notable increase in the alkaline phosphatase was observed on two occasions by O'Reilly.[11] This has previously been recorded as one feature observed in vitamin A poisoning but has not generally been mentioned.[19] Investigations into the blood-clotting mechanism have not been mentioned in other reports.

Radiologic Observations

Roentgenographic changes may be pathognomonic. Characteristic shadows of external thickenings of the corticallis, in many instances lamellated, have been observed regularly in the mandible, scapula, clavicles, ribs, humerus, tibia and ulna, and occasionally in the fibula and radius, metatarsals and calvarium.[3, 9] The ribs, long bones, and in some the clavicles may show pathognomonic lesions with visible soft tissue swellings. The metaphysis of tubular bones are unaffected and the spongiosa, epiphysis, epiphyseal plates and ossification centers are normal. Thickened pleura may be coincident with involvement of the ribs. Soft tissue swellings may occur prior to roentgenographic evidence of disturbance in bone.

Differential Diagnosis

Syphilis, scurvy, rickets and tuberculosis of bone may be excluded by associated clinical findings, specific laboratory tests and the generally characteristic lesions seen in roentgenograms. Erythroblastic anemia, leukemia, prematurity, traumatic or nontraumatic ossifying periostitis and periosteal lesions associated with prenatal bowing of the long bones might conceivably cause occasional confusion.

Atypical parotitis must be considered in those infants with facial edema[5] but may be satisfactorily excluded by the clinical associations and absence of typical osseous lesions. Conceivably acrodynia could also be a temporary cause for concern.[2]

Treatment

Treatment of early infantile cortical hyperostosis is empiric and expectant and is directed toward symptomatic relief. The disease appears to be self-limited with spontaneous recovery in all cases. The duration of symptoms in reported cases has ranged from 1 to 9 months. In the older children, because of the resemblance to hypervitaminosis A, reduction of dosage of vitamin A appears desirable. Relief of all symptoms has been reported to follow within a few weeks, though periosteal lesions may persist longer.

Summary

The coexistence of postinfantile hyperostosis and subdural hematoma, an association hitherto unreported, it described in a child 29 months old and a brief review of the 32 previously reported cases of infantile and postinfantile cortical hyperostosis is presented.

The cause of the syndrome is not known but hereditary, infectious, traumatic, allergic and hematologic factors have been considered. Hypervitaminosis A appears to be a definite etiologic possibility in the postinfantile form.

Hyperirritability, fever and anemia with leukocytosis are the outstanding clinical manifestations; characteristic shadows of external thickenings of the corticallis of the bones are pathognomonic.

Since the course of the disease is self-limited, treatment is directed toward symptomatic relief and reduction of intake of vitamin A when it has been excessive.

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SPANISH ABSTRACT

Hiperostosis Cortical Postinfantil con Hematoma Subdural; Informe de un Caso y Revista de la Literatura

La coexistencia de la hiperostosis postinfantil y el hematoma subdural, una combinación hasta la fecha no reportada en la literatura médica, se ejemplifica en el presente caso de una niña de 29 meses de edad. Una breve recopilación de 32 casos de hiperostosis cortical infantil y postinfantil, previamente reportados, se presenta en éste trabajo.

La cáusa del síndrome no es conocida, pero factores hereditarios, infecciosos, traumáticos, alérgicos, y hematológicos, han sido considerados. La hipervitaminosis A parece ser una posibilidad definitiva en la forma postinfantil.

Hyperirritabilidad, fiebre y anemia, con leucocitosis, son las manifestaciones clínicas sobresalientes; las sombras de engrosamiento externo de la corteza ósea son patognomónicas.

Como el curso de la enfermedad es limitado de su propia naturaleza, el tratamiento se dirige hacia el alivio de los síntomas, y la reducción en la ingestión de la vitamina A, si ésta ha sido excisiva.

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ABSORPTION OF FAT AND VITAMIN A IN PREMATURE INFANTS

I. Effect of Different Levels of Fat Intake on the Retention of Fat and Vitamin A

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A RECENT communication[1] by the authors reported that in cystic fibrosis of the pancreas and in the celiac syndrome the retention of fat was directly related to the quantity of fat provided in the diet. Thus, increasing the fat intake resulted in a correspondingly larger amount of fat retained by the body. It was further demonstrated that the increased quantity of feces, following the use of a high fat diet, did not bring about any greater loss of minerals or nitrogen than that which occurred with the use of a diet containing an average amount of fat. The results of these studies, therefore, indicated that the caloric loss in steatorrhea associated with cystic fibrosis of the pancreas and with the celiac syndrome could be met by including larger amounts of fat in the diet. Experience was cited that such a diet did not impair fat tolerance and was followed by favorable clinical results. Altogether similar were the authors' experiences in administering liberal quantities of fat in the treatment of infantile diarrhea.[2,3] It was found that higher levels of intake resulted in higher absolute retentions, the percentage retention showing no conspicuous change. The clinical experiences here were in accord with the metabolic data, being more favorable on a more liberal intake.

The present study was undertaken to ascertain whether this same situation obtained in the steatorrhea found in the premature infant. A study was planned of the retention of fat in premature infants following the administration of low and high fat diets. Information of this kind would not only be of academic interest, but would also be of practical importance, inasmuch as many pediatricians, following the recommendation of Gordon and Levine[4] and of Powers[5] prescribe diets low in fats for premature infants.

It was also thought worth while to ascertain the effect of low and high fat intakes on the excretion of vitamin A. Some clinicians are of the opinion that with a high fat intake a larger amount of vitamin A in excreted in the stools. However, as far as is known, no experimental evidence has been brought forth to substantiate this point.

EXPERIMENTAL PROCEDURES

Eight healthy premature infants, 11 to 28 days of age and weighing 1.3 to 1.8 kg., were used for this study. The infants were selected indiscriminately as to sex and color, but included only those known to consume all their feedings. At the beginning of the study an attempt was made to select

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* Mead Johnson fellow in pediatrics.

TABLE 1

DATA ON FAT RETENTION IN 8 PREMATURE INFANTS RECEIVING LOW AND HIGH FAT FEEDINGS

Case	Period	Age Days	Wt. gm.	Fat Intake Gm./Day	Fecal Fat Gm./Day	Fat Retention	
						Gm./Day	Per Cent Intake Retained
54	1	28	1440	4.2	1.38	2.82	67.2
	2	32	1650	16.8	6.96	9.84	64.5
	3	36	1750	4.2	2.35	1.85	43.5
58	1	11	1480	3.6	0.65	2.95	81.9
	2	15	1600	14.4	2.04	12.36	85.8
	3	19	1700	3.6	0.66	2.94	81.7
59	1	12	1480	3.3	1.09	2.21	67.0
	2	16	1640	8.4	3.28	5.10	60.7
	3	20	1600	3.3	1.32	1.98	60.0
60	1	13	1320	3.6	0.93	2.67	74.2
	2	17	1360	10.8	2.72	8.08	74.7
	3	21	1450	3.6	0.98	2.62	72.8
61	1	12	1840	5.4	1.13	4.27	79.0
	2	16	1900	16.2	2.63	13.57	83.7
	3	20	2000	5.4	0.98	4.42	82.0
62	1	11	1800	5.4	3.12	2.28	42.3
	2	15	1890	16.2	7.74	8.46	52.2
	3	19	1920	5.4	2.53	2.87	53.2
63	1	26	1560	3.6	1.0	2.60	72.3
	2	30	1640	10.8	0.92	9.88	91.3
	3	34	1750	3.6	0.78	2.82	78.4
64	1	20	1540	3.6	1.93	1.67	46.4
	2	24	1640	10.8	4.32	6.48	60.0
	3	28	1700	3.6	2.22	1.38	38.8
Average all infants	1	17	1558	4.08	1.40	2.68	65.7
	2	21	1665	13.05	3.82	9.22	70.7
	3	25	1734	4.08	1.48	2.60	63.7

the smallest prematures in the nursery as the impression was that they would be the poorest fat absorbers. However, as the study progressed, it was discovered that the poorest fat absorbers were not necessarily the infants who weighed the least.

The experiment was divided into 3 periods, each period being 4 days in duration. The fat content of the diet was low during the 1st and 3rd periods and high during the 2nd period. The diet* in the 1st and 3rd periods was identical and consisted of formulas prepared from butter fat, skimmed milk, corn syrup and water supplying approximately 120 cal./kg. body weight. The fat content of this diet

* The feedings used in this study were made available through the courtesy of Sheffield Farms, New York City, and National Dairy Products Laboratories, Sayville, Long Island. Measured amounts of butter fat (cream) and a fish liver oil preparation (oleum percomorphum) were homogenized with skimmed milk under 3500 lbs. pressure.

was 2% and provided approximately 20% of the total calories for the day. This amount of fat has been recommended by Gordon and Levine for the feeding of premature infants. In the 2nd period the fat content of the diet was increased to 6 or 8%. One cc. of a fish liver oil concentrate, oleum percomorphum, was homogenized in each quart of milk used for preparation of formulas in all 3 periods.

Stools were collected in plastic diapers (vinylite sheets). This method was found satisfactory as the stools could be readily separated from this material. The beginning and end of each period was identified in the stool by the appearance of ingested charcoal or carmine. A team of nurses trained in metabolic work was in charge of these infants during the entire study.

Each 4 day stool collection was weighed and an aliquot, after thoroughly mixing the stool, was used for vitamin A determination. The remainder was dried and the fat content was determined by the method of Tidwell and Holt.[6] Samples of milk were tested for fat content by essentially the same method after preliminary digestion with sulphuric acid. The vitamin A content of the formulas, as well as of the feces, was determined by the method described in a previous investigation.[7]

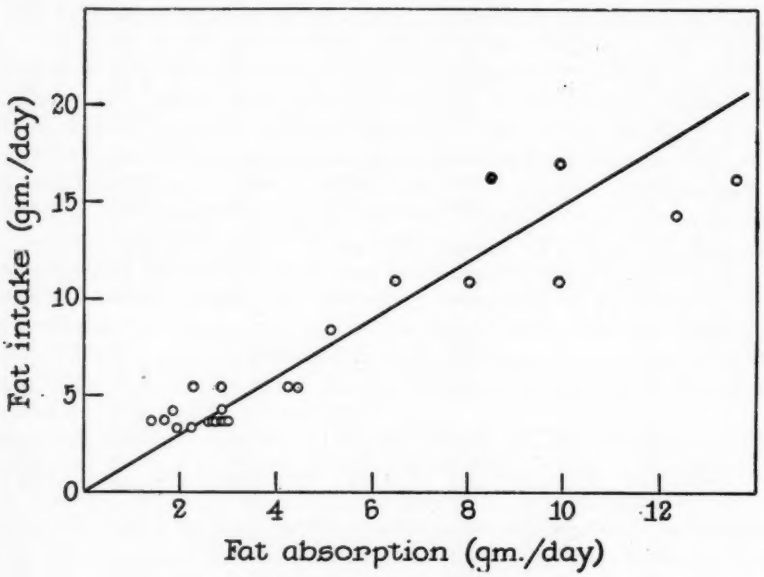

CHART 1. Relationship of fat intake to absorption.

RESULTS

In table 1 are recorded the amounts of fat retained by the premature infants following low and high fat feedings. It will be noted that during the periods of low intake there was considerable excretion of fat in the stools. Thus, the average excretion during the first period was 34.3% of the intake and during the third period, 36.3%. The amount of fat retained was therefore only 65.7% during the first and 63.7% during the third period. It may be recalled that the normal full term infant retains 85% to 95% of the fat intake. The data obtained during the first and third periods are consistent with those reported in the literature[8–10] and demonstrate the striking impairment of fat absorption in the premature infant.

In the second period, when the fat intake was increased three to four-fold, the amount of fat excreted in the stools was, as expected, larger than during periods one and three. However, the amount of fat retained by the premature infant was also considerably

higher following the administration of large amounts of fat. Thus, during the first and third periods, the average retention of fat per day per infant was 2.68 and 2.60 gm., respectively, whereas, during the second period, the infants retained an average of 9.22 gm. per day. In spite of the high fat feedings, the percentage of fat retained by premature in-

TABLE 2

DATA ON VITAMIN A RETENTION IN 8 PREMATURE INFANTS RECEIVING LOW AND HIGH FAT FEEDINGS

Case	Period	Fat Intake	Vit. A Intake	Fecal Excretion u./Day	Vit. A Retention	
					u./Day	Per Cent Intake Retained
54	1	Low	25,620	17,220	8,400	33
	2	High	15,540	7,166	8,374	54
	3	Low	25,620	8,357	17,263	68
58	1	Low	21,960	5,028	16,932	77
	2	High	13,320	2,150	11,170	85
	3	Low	21,960	4,352	17,608	82
59	1	Low	20,130	4,853	15,277	76
	2	High	12,210	5,640	6,570	54
	3	Low	20,130	7,192	12,938	65
60	1	Low	2,520	270	2,250	90
	2	High	3,780	1,065	2,715	73
	3	Low	2,520	1,054	1,466	60
61	1	Low	3,780	264	3,516	93
	2	High	5,670	717	4,953	88
	3	Low	3,780	717	3,063	79
62	1	Low	3,780	525	3,255	86
	2	High	5,670	3,403	2,267	40
	3	Low	3,780	993	2,787	74
63	1	Low	2,520	707	1,813	72
	2	High	4,240	300	3,940	93
	3	Low	2,520	427	3,353	89
64	1	Low	2,520	1,632	888	40
	2	High	4,240	1,716	2,524	60
	3	Low	3,780	2,191	1,589	44
Average all infants	1	Low	10,350	3,810	6,540	63
	2	High	8,080	2,770	5,310	65
	3	Low	10,510	3,160	7,350	69

fants was approximately the same as that which occurred following the use of low fat diets, the average retention being 65.7%, 70.7% and 63.7% during periods one, two and three, respectively. The direct linear relationship between fat intake and absorption is well illustrated in chart 1.

In table 2 are recorded the data on the relationship of the quantity of fat in the diet to

vitamin A absorption. Although it was planned to administer the same amount of vitamin A during the low and high fat feedings, assay of the milk containing the fish liver oil concentrate revealed that the vitamin A content was not constant throughout these periods. Nevertheless, the amounts of vitamin A administered to each premature infant were of the same order during the low and high fat feedings. It will be noted that the absorption of vitamin A varied considerably among the eight prematures. However, it is clear that the high fat feedings had no deleterious effect on the absorption of the vitamin. As is shown in the table, the average absorption of vitamin A during period two (high fat diet) was 65% of the intake, and during periods one and three (low fat diet), the absorption was 63 and 69%, respectively.

The relationship of vitamin A intake to absorption is shown in chart 2. It will be

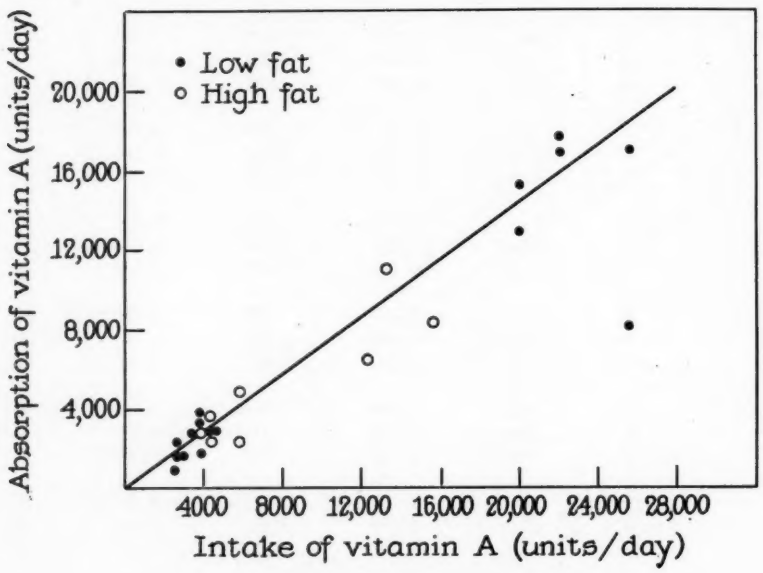

CHART 2. Relationship of vitamin A intake to absorption.

noted that, irrespective of the level of fat ingested, with increasing amounts of vitamin A there is a corresponding increase in the total absorption of the vitamin. This curve is similar to that obtained for fat absorption and indicates that the same relationship between intake and absorption holds for oily preparations of vitamin A as for fat.

COMMENT

The data in this investigation indicate that the percentage of the fat intake absorbed by the premature infant is the same whether the fat is administered in high or low amounts. Thus, increasing the amount of fat in the diet results in a correspondingly larger net absorption of fat. Therefore, the same principle of fat absorption holds for the premature infant as for acute diarrhea, cystic fibrosis of the pancreas and for the celiac syndrome. The reduction of the fat content of the diet in these conditions is unwarranted from a metabolic point of view.

It is not proposed at this time to advocate the routine administration of 6 or 8% butter fat in the formulas of premature infants. These high concentrations of butter fat were used in order to ascertain how well the intestinal tract of premature infants could absorb those large amounts of fat. The results indicate that the premature infant with marked steatorrhea not only absorbed considerable amounts of fat when the fat content of the diet was increased three to four-fold, but also tolerated these increases very well. In no instance was vomiting, diarrhea or anorexia noted. The clinical and metabolic results with the use of high fat feedings warrant a further trial on a much larger group of infants and, if the clinical results are just as satisfactory, higher fat diets might be recommended for premature infants. Certainly the traditional fear of prescribing butter fat in the same concentration as is used in formulas of full term infants is unfounded. In the premature unit here, it has been customary for many years to use formulas in which 40% of the caloric value was in the form of fat, an amount double that advocated by Levine and Gordon, and the clinical results have been very satisfactory.

The reduction to a minimum in the volume and weight of the food given to premature infants has generally been regarded as desirable. In this connection it may be pointed out that because of its higher caloric value the use of fat permits a smaller intake of food by weight, despite the inefficient absorption of fat. Assuming that protein and carbohydrate absorption are normally efficient (circa 90%) it would be necessary for fat absorption to fall below 40% before it reached the low level of absorbed calories/gm. of food provided by the other two foodstuffs; experience shows that such a low fat absorption rarely prevails.

In regard to the effect of high fat feedings on the absorption of vitamin A, the data indicate that the absorption was the same whether the diet contained high or low amounts of fat. The average vitamin A absorption was 65% following a high fat and 66% following a low fat diet. This degree of vitamin A absorption is quite high when one recalls that in the full term infant, 62% of vitamin A is absorbed with the administration of an oily preparation. It should be emphasized, however, that in the present experiment the oil was homogenized in milk whereas the data on full term infants were obtained following the direct administration of unemulsified oil. It has been shown in a previous paper[11] that a homogenized emulsion of fish liver oil greatly enhances the absorption of vitamin A. A forthcoming report[12] will discuss the important role of particle size in the absorption of fat and vitamin A in premature infants.

Summary

Eight premature infants manifesting steatorrhea were placed on diets containing low and high amounts of fat in order to ascertain how economically the premature infant could utilize large amounts of fat. At the same time the effect of administering large amounts of fat on the vitamin A absorption of premature infants was investigated. The results of these studies indicated that in spite of steatorrhea the percentage of fat absorbed was essentially the same whether the diet contained high or low amounts of this food. Thus, the net absorption of fat was correspondingly higher following the use of a high fat diet. The absorption of vitamin A was approximately the same following the low or high fat regimen.

The finding that relatively high fat diets given to premature infants not only result in better fat retention but are also well borne clinically suggests that the currently advocated restriction of fat in these subjects is unnecessary and possibly undesirable.

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SPANISH ABSTRACT

Absorción de Grasa y Vitamina A en Infantes Prematuros. I. Efecto de Diferentes Cantidades de Toma de Grasa en la Retención de Grasa y Vitamina A

Ocho infantes prematuros con manifestaciones de esteatorrea fueron colocados en dietas conteniendo cantidades bajas y altas de grasa para ascertar cuan economicamente el infante prematuro podía utilizar grandes cantidades de grasa. Al mismo tiempo se investigó el efecto de la administración de grandes cantidades de grasa en la absorción de vitamina A de los infantes prematuros. Los resultados de estos estudios indicaron que a pesar de la esteatorrea el porcentaje de grasa absorbida fué esencialmente el mismo ya fuera que la dieta contuviera cantidades altas o bajas de este alimento. Así, la absorción neta de grasa fué correspondientemente más alta después del uso de una dieta de alta grasa. La absorción de vitamina A fué aproximadamente la misma después de un régimen de grasa bajo o alta.

El descubrimiento de que las dietas relativamente altas en grasa dadas a infantes prematuros no solamente resultan en mejor retención de grasa, sino que también se llevan bien clinicamente, sugiere que es innecesaria y posiblemente desventajosa la restricción de grasa corrientemente recomendada en estos sujetos.

477 First Avenue

DETERMINATION OF THE OXYGEN CONTENT OF CAPILLARY BLOOD IN CONGENITAL HEART DISEASE

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ONE of the most valuable measurements that can be made in a study of a patient with congenital heart disease is an accurate determination of the oxygen content of a sample of arterial blood removed under conditions of rest. Such a determination has a threefold usefulness:

1. It may differentiate between a cyanotic and noncyanotic lesion. 2. It can give some estimate as to the degree of severity of a cyanotic lesion. 3. It enables one to follow changes in oxygen unsaturation produced by exercise or surgical therapy.

However, in small children, the technic of arterial puncture is sometimes difficult and usually accompanied by considerable pain and discomfort. The value of the determination may be decreased by the conditions of fright and struggle under which it was drawn. For these reasons blood oxygen studies are seldom made in many clinics and a valuable piece of information is not available.

On the other hand, the unreliability of visual estimates of cyanosis is well known and has been recently demonstrated.[1]

Many years ago it was known that capillary blood obtained from the finger tip was identical in oxygen content with arterial blood.[2] Clinicians failed to take advantage of this fact at that time because of the difficulty of collecting the samples under oil and the lack of an accurate method of measuring the oxygen content in small samples of blood. In 1944 Lilienthal and Riley[3] collected samples of capillary blood from an ear lobe previously warmed by radiant heat and measured their oxygen content by the microgasometric technic of Roughton and Scholander. The collection system did not involve the use of oil, was simple and efficient, and the analysis of oxygen content and capacity could be made on samples of 0.4 to 0.5 ml. of blood. Using this technic in 11 subjects, they compared capillary blood samples with arterial blood samples analyzed by the Van Slyke method and found a maximum error of 3.1% in oxygen saturation. Variations in arterial oxygen content were induced by breathing various mixtures of oxygen and nitrogen. Lawrence,[4] in a study of blood oxygen in patients with polycythemia, found the oxygen content of capillary blood to be within 0.5 volumes per cent of arterial blood in 19 out of 25 subjects. However, in one instance a difference of 3.3 volumes per cent was found. All analyses were made by the technic of Roughton and Scholander.

In the past year a modification of the method of Lilienthal and Riley has been used on the pediatric wards of Stanford University Hospital in the study of children with congenital heart disease. In over a hundred examinations the method has proved simple and

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accurate, and it can be performed quickly with minimum disturbance to the patient. The purpose of this paper is to describe the method used at the Stanford Hospital and in addition to present a comparison between the oxygen content of capillary blood collected and analyzed by this technic and simultaneously drawn samples of arterial blood analyzed in the conventional manner.

Method

A 5 ml. luer type syringe with a glass tip is employed (see fig. 1). The bore of the glass tip is ground out slightly so that a tight fit can be made between it and the tip of the

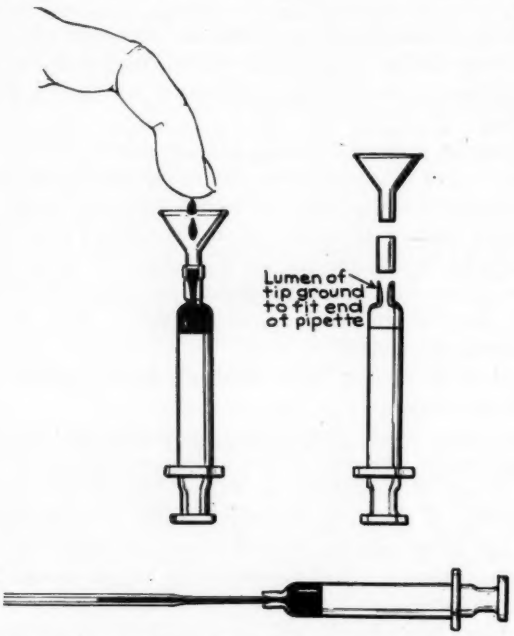

Fig. 1. Sketch of blood collection apparatus showing assembly and manner of use. Lower drawing shows how Roughton-Scholander pipette is loaded.

Roughton Scholander pipette. For ease of fine adjustment the syringe barrel and plunger are coated lightly with stopcock grease. A small glass funnel, which can be made by any glassblower, is fitted to the syringe tip by a short sleeve of plastic tubing. To prevent clotting and reduce the tendency for the blood to smear or spread in a film, the inside of the funnel and syringe is coated with silicone.[5] The inside of the syringe is moistened with a drop or two of heparin, the excess is expelled, and prior to collection a drop of mercury is placed in the neck of the funnel.

It has been found more convenient to use blood from the finger tip. In children with clubbing an especially prompt flow of blood can be obtained. The entire hand to 6 inches above the radial styloid is immersed in a pan of water at 47°C. for 10 minutes. In small children a hot compress wrapped in a towel will suffice. This causes vasodilation so that the venous blood will approach the arterial blood in its oxygen content.[6] In some very young children the heel can be used after compressing the entire foot. The ball of the

index or middle finger is usually selected. It is cleansed with alcohol and then coated lightly with carbolated vaseline which prevents the blood from smearing. Usually a single, deep 4 mm. jab with a new number 14 Bard Parker blade will result in a prompt and copious flow of blood. The first few drops are discarded. The finger is then held without squeezing by an assistant directly over the collecting funnel so that the blood falls only 1 or 2 cm. through the air. As the blood drops into the funnel, the syringe barrel is carefully pulled down with a screwing motion so that the blood is drawn steadily into the barrel without the admission of air droplets. The momentary exposure of the drops of blood to the air during collection does not change the oxygen content of the sample. When 0.5 cc. of blood has been collected, the funnel and plastic sleeve are removed and any air bubbles in the syringe are carefully squeezed out. The tip is then plugged by a round toothpick and the syringe shaken for 3 minutes, the mercury serving to agitate the blood. The sample is then placed in a refrigerator at 0°C. A gauze pad is placed over the puncture site and held in place by tape.

It is important to obtain a free flow of blood. If squeezing is necessary, it is better to select another puncture site and repeat the procedure. Difficulty has occasionally been encountered in postoperative patients who have lost blood or who are in shock. It may be necessary in such cases to make a somewhat deeper cut to obtain an adequate sample.

In some instances as much as 3 or 4 cc. of blood may be obtained and the oxygen analysis can be carried out in the standard Van Slyke apparatus if this is more convenient.

It is best to perform the analysis the same day. At 0°C. no change in oxygen content has been noted up to 6 hours. Samples left overnight usually show a fall of from 1 to 2 volumes per cent in oxygen content.

In studying children with polycythemia it is best to use the 50 cmm. size analyzer. After thoroughly agitating the sample the toothpick is removed and the first few drops of blood are discarded. The tip of the Scholander pipette is placed in the enlarged bore of the syringe tip, and if a tight connection has been made the pipette can easily be loaded. The determination is then made in the Roughton Scholander analyzer in the usual manner.[7] It requires practice and patience before the necessary skill is developed to obtain accurate results in this analysis. It is best to have available a standard Van Slyke apparatus so that frequent checks on larger samples of blood can be made from time to time. In the hands of a skillful operator the determination can be made within the limits of $\pm$ 0.2 volumes per cent. The entire analysis, including the determination of the oxygen capacity, should not require longer than an hour.

When the oxygen content has been measured, the plunger of the syringe is withdrawn so that an air space of 2 cc. is present. The sample is then gently agitated for 20 minutes. The air should be changed twice during this time. Air is then expelled and the determination of the oxygen capacity is made, using the same technic. In addition it is valuable to determine the hemoglobin content of the sample and, if enough blood is available, to measure the packed cell volume. This will serve as an added check on the accuracy of the oxygen capacity determination.

Normal subjects will have a capillary oxygen saturation of from 92 to 96% as determined by this method.

In order to test the accuracy of the method, studies were made of 10 patients with various levels of hemoglobin and oxygen saturations. Adult subjects were selected because of the greater ease of arterial puncture. Capillary blood was drawn from the finger and analyzed as described. At the same time a sample of blood was drawn from the brachial

TABLE 1 (a)

COMPARISON OF ANALYSES OF CAPILLARY AND ARTERIAL BLOOD IN 10 SUBJECTS

Case No.	Diagnosis	Age Yr.	Hgb. Gm. %	O_2 Content Vols. %		Diff Vols. %	% Error	O_2 Capacity Vols. %		Diff Vols. %	% Error	% Sat.
				Cap.	Art.			Cap.	Art.			
1	Carcinoma of stomach	53	7.8	9.8	9.6	+.2	2.1	10.6	10.5	+.1	.9	92
2	Diabetes mellitus	32	13.2	14.3	14.5	−.2	1.4	15.9	16.0	−.1	.6	91
3	Chronic duodenal ulcer	59	13.7	17.2	17.0	+.2	1.2	18.1	18.2	−.1	.6	93
4	Cardiovascular syphilis with aortic insufficiency	49	14.0	17.3	17.6	−.3	1.7	19.0	19.4	−.4	2.1	91
5	Cerebrovascular accident	61	14.6	20.0	20.3	−.3	1.5	20.5	20.5	0	0	99
6	Hypertensive cardiovascular disease	78	15.0	18.2	18.3	−.1	0.6	20.8	20.8	0	0	88
7	Hypertension	36	15.0	19.6	19.7	−.1	0.5	20.7	20.6	+.1	.5	95
8	Duodenal ulcer	50	15.9	21.0	21.0	0	0	22.4	22.4	−.4	1.8	94
9	Pulmonic stenosis; Interauricular septal defect	24	20.5	20.6	20.8	−.2	1.0	29.6	29.5	+.1	.3	70
10	Tetralogy of Fallot	15	24.2	23.2	23.3	−.1	0.4	32.3	32.4	−.1	.3	72

Maximum difference 0.4 vol. %
Maximum per cent error 2.1%

TABLE 1 (b)

11	Chronic bronchitis	63	16.1	16.6	17.4	−.8	4.6	21.8	21.9	.1	.5	80
12	Essential hypertension	36	16.1	18.4	20.9	−2.5	12.0	21.8	21.7	+.1	.5	96

artery, and the oxygen content and capacity was measured in a Van Slyke apparatus. The close comparison of the results can be seen in table 1 (a). The maximum difference was 0.4 volumes per cent, an error of 2.1%.

In two subjects, table 1 (b), the technic of blood collection was faulty. Only a small sample was obtained, and during the process the finger was squeezed firmly several times. A difference of as much as 2.5 volumes per cent was obtained. This probably represented contamination of the sample with venous blood and not with tissue juice since the oxygen capacities were equal.

Table 2 summarizes a representative series of observations made on children of various

TABLE 2

ANALYSES OF CAPILLARY BLOOD IN CASES OF CONGENITAL HEART DISEASE

Case No.	Diagnosis	Age Yr.	Hgb. Gm. %	Cyanosis	Clubbing	Symptoms	O_2 Content Vol. %	O_2 Capacity Vol. %	% Sat.
13	Pulmonic stenosis with interauricular and interventricular septal defects	7	19.3	+	++	++	19.5	26.2	75
14	Cyanotic variety of congenital heart disease	12	19.0	++	++	++	19.6	25.4	77
15	Tetralogy of Fallot	2	16.1	+++	+++	+++	13.7	21.7	63
16	Tetralogy of Fallot	3	14.8	+++	+++	+++	11.4	20.0	57
17	Complete transposition of great vessels	2	16.5	+++	+++	+++	7.8	22.3	35
18	Tetralogy of Fallot	16 mos.	17.8	+++	+++	+++	4.0	24.0	17
19	Tetralogy of Fallot	9	26.0	++	+++	++	20.3	33.7	60
20	Tetralogy of Fallot	4	12.0	+	+	++	11.8	15.4	77
21	Tetralogy of Fallot	20	12.0	+	+	+	12.0	16.2	74
22	Newborn		16.2	+	0	0	16.7	21.5	78
23	Eisenmenger's syndrome	3	12.0	0	0	0	12.9	15.2	85
24	Tetralogy of Fallot	4	19.1	+	+	+	19.9	24.0	83

ages and with various congenital lesions. No arterial blood samples were drawn in this group.

There are two principal sources of error in using the method: 1. Faulty collection of blood. If a free flow cannot be obtained, another puncture site should be selected. 2. Error in analysis. This can be controlled by making frequent checks on larger samples of blood analyzed for oxygen content in a Van Slyke apparatus.

SUMMARY

A previously described technic of collecting and analyzing capillary blood for oxygen content has been modified slightly and applied in the study of children with congenital heart disease. Samples obtained and analyzed in this manner differed in oxygen content from simultaneously drawn arterial samples by no more than 0.4 volumes per cent. The value of the technic in the study of congenital heart disease has been illustrated.

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SPANISH ABSTRACT

Determinación del Contenido de Oxígeno de Sangre Capilar en Enfermedad del Corazón Congénita

Una técnica descrita anteriormente para coleccionar y analizar sangre capilar para el contenido de oxígeno ha sido ligeramente modificada y aplicada en el estudio de niños con enfermedad del corazón congénita. Las muestras obtenidas y analizadas en esta manera no difieren en contenido de oxígeno de aquellas muestras arteriales simultaneamente sacadas más que 0.4 volumenes por ciento. El valor de la técnica en el estudio de la enfermedad del corazón congénita ha sido ilustrado.

Clay and Webster Streets

DIASTEMATOMYELIA (CONGENITAL CLEFTS OF THE SPINAL CORD)

Diagnosis and Surgical Treatment

By DONALD D. MATSON, M.D., ROBERT P. WOODS, M.D., JAMES B. CAMPBELL, M.D., AND FRANC D. INGRAHAM, M.D.
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INTRODUCTION

ASSOCIATED with congenital abnormalities of the neural axis, simultaneous faulty development of surrounding mesodermal structures is prone to occur. This error of embryologic growth is manifested in a wide variety of clinical entities extending from the simplest type of asymptomatic lumbosacral spina bifida occulta to complete spinal rachischisis. At either extreme, these instances of spinal "dysraphism"[1] are of little or no clinical significance, since at one extreme no therapy is necessary and at the other, none is either possible or desirable. There is a wide range of conditions between, however, in which surgical treatment is indicated; these include meningoceles, certain myelomeningoceles, congenital dermal sinuses and some varieties of spina bifida occulta.

It is the purpose of this report to describe a number of patients in whom an unusual type of occult spinal disorder has been recognized and treated surgically in early childhood. These cases may be grouped together under the designation diastematomyelia, a term which actually includes any abnormal cleft or division of the spinal cord or its intraspinal derivatives. Multiple congenital anomalies of the vertebrae, including some degree of incomplete spinal fusion, were present in every instance. However, the distinguishing feature in this group of patients was the projection of a discrete bony spicule from the posterior surface of a vertebral body through the spinal canal to transfix the spinal cord or cauda equina, usually in the midline.

The majority of observations on diastematomyelia have been reported as postmortem descriptions of stillborn monsters or grossly deformed infants. In such instances extensive division of the spinal cord was usually associated with large fusion defects of the overlying mesodermal structures so that myelomeningoceles, spinal rachischisis and hydrocephalus were usually present and responsible for death in the early postnatal period. Diagnosis of less severe degrees of diastematomyelia during life has been infrequent and with the exception of one case[2] its recognition preoperatively followed by a planned surgical attack hitherto unreported. This paper presents the authors' experience with two cases discovered inadvertently at the time of laminectomy and nine cases, all seen since 1946, in which the diagnosis was made preoperatively and surgical therapy employed.

LITERATURE

No attempt will be made to summarize the embryologic and pathologic literature dealing with diastematomyelia in this clinical report. The review of Herren and Edwards in

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1940[3] is well-documented. Lichtenstein[1] described diastematomyelia as an "example of the dysraphic state to an extreme degree" but pointed out that cases have been reported in which the neural anomaly was not associated with a bone defect.

There have been few reports of operative cases. Maxwell and Bucy[4] described a 9 months' old girl who was operated upon for a congenital dermal sinus in the lumbar region. Exploration revealed separation of the cord into two halves with each half enclosed in its own dura below the level of L_3. There was a bony spicule separating the two dural compartments. Hamby[5] reported a 20 year old female in whom the cord was transfixed at L_3 by a bony spicule. This patient had also a pilonidal sinus and spina bifida occulta. Herren and Edwards[3] described a 23 year old Negro female in whom a paraparesis was present. At exploration a bony spicule was disclosed transfixing the contents of the spinal canal. There was temporary improvement following decompression without removal of the bony spicule. This patient died because of a cerebral glioma.

A 12 year old girl was reported by Marr and Uihlein[6] in whom a bony spicule transfixing the cord at L_3 was removed with subsequent improvement of a mild paraparesis. A fifth case, described by Zalewska-Ploska,[7] was that of a 2 month old girl who died following exploration of a myelomeningocele with associated bifid cord. Walker[8] reported a patient whom he had explored expecting to find a congenital tumor because of widened interpedicular spaces by roentgenograms and instead found a divided spinal cord. In his case there was no bony spicule or dural septum between the two divisions of the cord.

Pickles[2] reported, in 1949, a 14 year old girl, studied because of progressive weakness

TABLE 1

No.	Name	Age	Level of Lesion	Cutaneous Defect	Neurologic Defect	Myelography	Operation	Follow-up
1	P.S.	3 3/12	T_{11}	Lipoma	Lower extremities. Both sphincters.	Not done	Mar. 1934	Unknown
2	E.H.	5 4/12	L_4	Tuft of hair	L.E.	Not done	June 1940	June 1947. No progression. Improvement with tendon transplant.
3	G.D.	1 6/12	L_4	Skin dimple	L.E.	Diagnostic	Aug. 1946	June 1949. No progression. Gait improved.
4	M.I.	2 10/12	T_8	None	L.E.	Not done	Feb. 1948	Aug. 1948. No change.
5	M.M.	8 wk.	L_4	Tuft of hair and telangiectasis.	None	Diagnostic	May 1948	May 1949. No abnormality.
6	S.S.	2 3/12	L_1	None	None	Diagnostic	July 1948	Sept. 1948. Continent. Asymptomatic.
7	R.A.	1 10/12	T_{10}	Skin dimple	L.E.	Diagnostic	Aug. 1948	June 1949. Much improved.
8	R.C.	4 8/12	T_{11}	Hemangioma. Tuft of hair	L.E. Poor sphincter control	Not done	Aug. 1948	Feb. 1949. Improved.
9	D.L.	4 mo.	L_2	Skin dimple. Tuft of hair.	Urinary incontinence	Diagnostic	Sept. 1948	March 1949. Improved.
10	J.M.	1 11/12	T_8	Lipoma	L.E.	Diagnostic	Oct. 1948	June 1949. Improved.
11	A.L.	5 9/12	L_4	Skin dimple. Lipoma.	L.E. Urinary incontinence	Diagnostic	Jan. 1949	June 1949. Improved.

of the right leg associated with both sensory and reflex changes. Myelography revealed a split in the oil column at T_{10} and a bony spicule projecting through the dura and dividing the cord at this level was found at operation. In none of these seven cases, except the last, was the diagnosis of diastematomyelia made previous to operation.

Material

As will be noted from table 1 and from the case reports, this material consists of 11 patients in whom diastematomyelia was diagnosed during life and treated surgically. There were 8 females and 3 males. The age of these patients ranged from 8 wk. to 5 yr., 9 mo. All were treated on the neurosurgical service of The Children's Hospital. Most of them had originally been seen in the orthopedic or surgical departments and transferred after the proper diagnosis was made. A keen interest by the radiologists of The Children's Hospital in the diagnosis of this lesion on plain roentgenograms (RGs) and by myelography has been of invaluable aid in the management of these patients.

Case Reports

Case 1. P. S., a 3 3/12 yr. old boy, was admitted because of persistent urinary incontinence, rare fecal incontinence and the history of a club foot since birth. Examination revealed a fat pad over the lumbar spine, a midline skin dimple, displacement of the 2nd and 3rd toes on the right foot and absent deep tendon reflexes in both legs. RGs showed multiple developmental deformities in all the lumbar and sacral vertebrae. Exploration revealed division of the spinal cord caudally from T_{10} by a bony septum. The left half of the cord was larger than the right. The child did well postoperatively but was not followed in this clinic.

Case 2. E. H., a 5 4/12 yr. old girl, was admitted because of difficulty in walking for 1 yr. Examination showed a midline tuft of hair in the sacral area, atrophy and shortening of the left leg and a cavus deformity of the foot. RGs revealed a lumbar spina bifida with widening of the interpedicular spaces. At operation a bony spicule arising from the body of L_4 divided the nerves of the cauda equina into 2 groups, each enveloped in its own meninges. Arachnoidal adhesions were separated and the spicule removed. There has been no apparent increase in the deformity of the lower extremities and the gait has been improved considerably by orthopedic procedures carried out in 1945.

Case 3. G. D., a 1 6/12 yr. old girl, was admitted because of inequality of leg size. Examination showed a midline sacral skin dimple, shortening and atrophy of the right leg, weakness of the right tibialis anterior and posterior and an absent ankle jerk. RGs showed a lumbo-sacral spina bifida with widening of the interpedicular spaces. "Pantopaque" myelograms disclosed a midline filling defect at the level of L_4. At operation a bony spicule at L_4 divided the dura into separate channels each containing about half the roots of the cauda equina. Numerous arachnoidal adhesions were divided and the bony spicule removed. Three years after admission the gait was still abnormal and atrophy still present, but there was definite improvement in the function of the tibialis anterior and posterior.

Case 4. M. I., a 2 10/12 yr. old girl, was admitted because of rapid increase in weakness of the lower extremities over a period of 6 wk. Examination revealed a marked spastic paraparesis, hyperactive deep tendon reflexes, inability to walk and a bilateral equinus deformity of the feet. RGs showed widening of the spinal canal from T_6 to T_{12} with a midline bony spicule visible at T_8. At operation, the spicule was found to split the dura into 2 separate channels. A large portion of the spicule was removed. Postoperatively the neurologic deficit was greater, with loss of sphincter control and almost no voluntary motion of the legs. A radical removal of the bony septum was therefore carried out, still extradurally, facilitated by sacrifice of 3 nerve roots. There was marked improvement immediately after operation and she continued slow improvement in voluntary motion during the next 3 mo.

Case 5. M. M., an 8 wk. old girl, was admitted because of a patch of hair in the lumbosacral region. Examination revealed no neurologic deficit. RGs showed widening of the lumbar interpedicular space with anomalies of the neural arches and a midline area of opacity at L_3. "Pantopaque" myelography showed a filling defect in the midline at this level. At operation a spicule was found dividing the cord and transfixing it so that the tip of the conus lay at S_1. There were normal lateral roots but no medial roots from the 2 divisions of the cord. Arachnoidal adhesions were divided and the spicule removed together with its dural investment. One year later there was no evidence of neurologic deficit and the child was developing normally.

Case 6. S. S., a 2 3/12 yr. old girl, was admitted because of fever, irritability and incontinence of

urine. She was stuporous, had flaccid extremities and showed 550 WBC in her spinal fluid. The child responded well to antibiotic and supportive therapy. RGs revealed widening of the vertebral canal in the thoraco-lumbar area with a small line of increased density over L_1 and an anomaly of the body of T_{11}. "Pantopaque" myelography showed a central filling defect at L_1. At operation a small dermoid cyst was encountered in the region of the rudimentary L_2 spinous process. At L_1 a bony and fibrous septum divided the dural canal. The dura was opened revealing a bifid cord extending down to the caudal margin of the septum where the 2 halves again reunited. Adhesions were divided and the septum removed. Four months later the child showed no neurologic deficit and was enjoying unlimited activity.

Case 7. R. A., a 1 10/12 yr. old girl, was admitted because of difficulty in walking. Examination revealed a lumbar pilonidal dimple, atrophy and shortening of the left leg, weakness of the left leg, absent deep tendon reflexes on the left and a bilateral calcaneo-valgus deformity of the feet. RGs showed spina bifida and widening of the canal at T_{10}-T_{11} with a bony spicule in the midline. "Pantopaque" myelography disclosed division of the column of the dye for a distance of 2 cm. At operation, a dura-enveloped spicule transfixed the cord at T_{11}. The cord reunited immediately caudal to the spicule. After dividing adhesions the septum was removed. Ten months later the reflexes were normal, voluntary motion in the left leg was improved and the child had been walking unassisted for 6 mo.

Case 8. R. C., a 4 8/12 yr. old boy, was admitted because of easy fatiguability, dragging of the right leg and an increase in enuresis over a 4 mo. period. Examination showed a 3 cm. port-wine stain with protruding long hairs in the midline of the thoraco-lumbar area, atrophy of the right thigh, pronated feet and diminished rectal sphincter tone. RGs showed multiple anomalies of the vertebrae from T_{10} to L_2 with widening of the canal and an oval area of increased density in the midline at T_{11}. At operation a bony septum divided the dura into 2 compartments at T_{11}. On opening the dura a bifid cord was visualized for several segments cranial to the spicule with union just caudal to it. All adhesions were divided and the spicule removed. Six months later there was no weakness but a questionably shuffling gait. Sphincter tone was improved.

Case 9. D. L., a 4 mo. old girl, was admitted because of an abnormal growth of hair in the lower lumbar region. On examination there was also a midline skin dimple, poor rectal tone and constant urinary dribbling. RGs showed widening of the lumbar canal with a midline narrow opacity at L_2. "Pantopaque" myelography confirmed a division of the subarachnoid space. At operation a midline, dura-enveloped septum of bone was found at L_2 anchoring the conus medullaris caudal to this point. A fibrous tract was also found leading from the skin dimple to a point of fixation amid the cords of the cauda equina. The septum was removed and the cord mobilized. The fibrous tract was also excised and proved to be a dermoid. Six months later there was definite improvement of sphincter control, no muscular weakness and an extensor plantar response on the right.

Case 10. J. M., a 1 11/12 yr. old girl, was admitted because of inability to walk unsupported. Examination showed a small fatty mass in the upper lumbar region, absent deep tendon reflexes in the lower extremities, but positive Babinski signs bilaterally, a spastic type of gait and pronation of the feet. RGs showed a lumbar spina bifida with anomalies of L_5 and the sacrum, spina bifida of T_7-T_9 with widening of the canal at this level and a midline linear opacity at T_8. "Pantopaque" myelogram showed a filling defect at T_7-T_8. At operation a dura-lined bony spicule transfixed the cord at T_8. After opening the dura and dividing adhesions from the medial surfaces of the bifid cord, the spicule and its dural reflections were removed. The 2 halves of the cord reunited immediately caudal to the spicule. Eight months later reflexes were present but diminished, spasticity was much less and walking was continuing to improve.

Case 11. A. L., a 5 9/12 yr. old boy, was admitted because of increasing weakness of the right leg and increasing lack of control of urination. Examination showed scoliosis, atrophy and shortening of the right leg, absent deep tendon reflexes and weakness of all muscle groups on the right, an equinovarus deformity of the right foot and a deep midline sacral skin dimple. RGs showed a lumbosacral spina bifida with multiple anomalies of the vertebral bodies. "Pantopaque" myelograms showed a linear eccentric filling defect at L_3-L_4. At operation a bony septum invested by dura completely divided the canal just to the right of the conus. About one third of the roots of the cauda equina passed down the right channel and the balance down the left. Some roots were deflected around the septum and coursed cranially again in order to reach their appropriate intervertebral foramina. After dividing adhesions, the septum was removed, allowing the conus and cauda equina to move freely. Immediate improvement was noted in bladder control. Five months later his gait had also improved and orthopedic rehabilitation was proceeding satisfactorily.

Diagnosis

As in many unusual disorders which are not immediately obvious on physical examination, the most important factor in diagnosis of diastematomyelia is awareness of the possibility of the lesion. Since this anomaly has come to the authors' attention in recent years, suspicion of the anomaly to a degree warranting careful roentgen study has frequently been rewarded by establishment of the diagnosis preoperatively.

Although all these cases of diastematomyelia were associated with occult spinal disorders in that no intraspinal contents were actually visible on the surface, in most of the

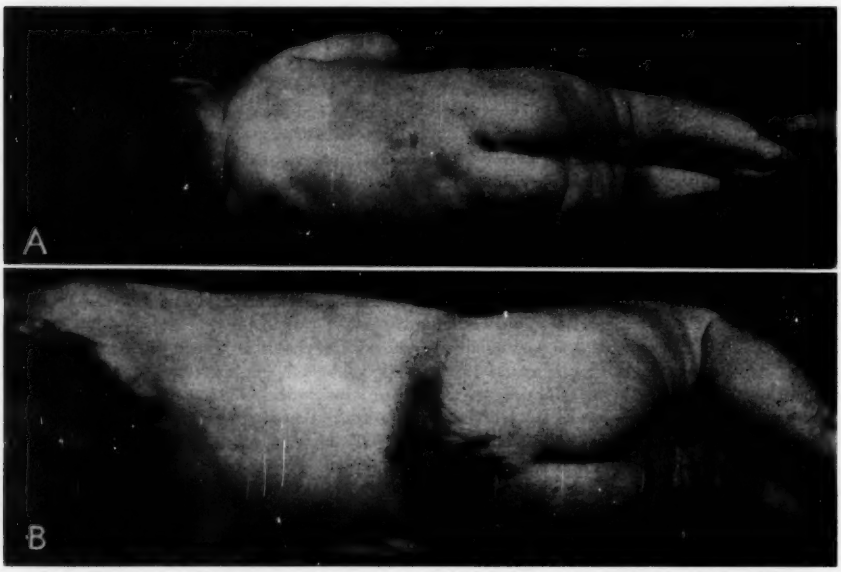

Fig. 1. A. Cutaneous angioma in lumbar region and midline sacral dimple in 4 mo. old girl (Case 9). Bony spicule at L_5 with division and fixation of spinal cord. B. Abnormal hair tuft in lumbar region in 8 wk. old girl (Case 5). Bony spicule at L_4 with division of cord and fixation of conus medullaris at S_1.

patients a cutaneous defect, usually in the midline, was present in the region of the underlying neural abnormality. The same variety of cutaneous defects were encountered as in other types of occult spinal disorders (Figs. 1 and 2). These consisted of abnormal tufts of hair (Cases No. 2, 5, 8, 9), skin dimples (Cases No. 3, 7, 9, 11), subcutaneous poorly circumscribed masses of fat (Cases No. 1, 10, 11) and port-wine stain or cutaneous angioma (Case No. 8).

It is obvious that the presence of skin lesions along the midline should alert the observer to the possibility of underlying neural or mesodermal anomalies. Two infants in this series, aged 4 and 8 months, respectively, were brought to the hospital primarily because of abnormal tufts of hair in the lumbosacral region before dribbling of urine and weakness of the lower extremities had become apparent. Detection of a cutaneous defect at any age should be followed by careful roentgen examination of the spine and by careful neurologic evaluation of the lower extremities. In early infancy midline bony spicules may

not be visible and spina bifida difficult to determine by roentgen examination. These studies should, therefore, be repeated at intervals as growth proceeds. If plain roentgenograms continue to be negative and there is any suggestion of neurologic impairment, myelography should be carried out.

The presenting complaints of the majority of these patients were based, not on cutaneous lesions, but on peripheral evidence of neurologic dysfunction. The most common disturbance was difficulty in walking or in learning to walk. These patients were usually referred by their pediatricians to an orthopedic surgeon for investigation of deformities of the lower extremities or of the gait (Figs. 2-5). Roentgenograms made of the spine in the course of this investigation revealed the nature of the lesion. There was no constant type of abnormality in the lower extremities in this group. One patient showed weakness of the right peroneals, tibialis anterior and posterior and the long toe flexors; the knee and ankle jerks were absent and the foot was held in equinovarus position (Case 11). A second patient showed bilateral weakness of the anterior tibial muscles, pronated feet and a spastic type of gait (Case 10). A third showed easy fatiguability and a tendency to drag his right leg though no specific muscle weakness could be determined (Case 8). A fourth showed atrophy of the left thigh, weakness of the tibialis anterior and posterior,

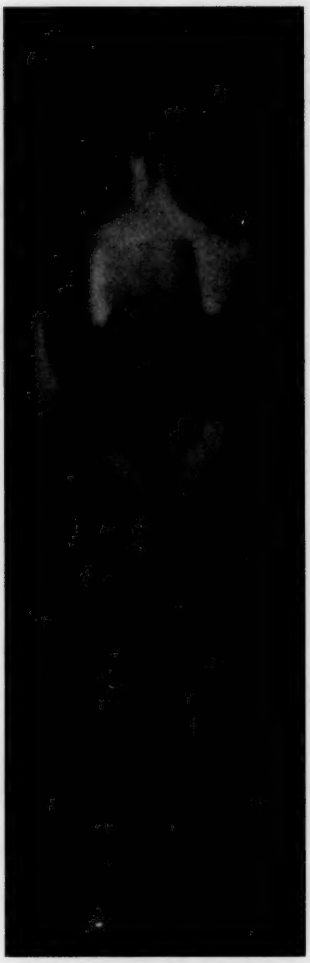

FIG. 2. Atrophy of right leg and pronation of both feet with dragging of right leg on walking in 4 8/12 yr. old boy. There are also cutaneous telangiectases and excessive hair in thoraco-lumbar area (Case 8). Bony spicule at T_{11} with complete division of cord.

bilateral calcaneo-valgus position of the feet and absent deep tendon reflexes (Case 7). A fifth showed an equinus deformity of both feet with a spastic gait (Case 4). A sixth showed atrophy and shortening of the right leg with weakness of the tibialis anterior and posterior and absence of the long flexors of the toes (Case 3). A seventh showed atrophy of the left calf with weakness of the flexors of the toes and a tendency to drag this foot on walking (Case 2). An eighth patient showed deformity of the toes and absent deep tendon reflexes bilaterally (Case 1). It seems evident, therefore, that many types of gait disturbance or deformities of the feet and legs may be present depending upon what type of muscle imbalance develops secondary to the neurologic lesion.

Sensory examination in this age group is difficult and unreliable and was rarely of help in this series. Urinary incontinence was the primary complaint in one patient (Case 1) and poor sphincter control was established on examination in four additional patients (Cases

Diagnosis

As in many unusual disorders which are not immediately obvious on physical examination, the most important factor in diagnosis of diastematomyelia is awareness of the possibility of the lesion. Since this anomaly has come to the authors' attention in recent years, suspicion of the anomaly to a degree warranting careful roentgen study has frequently been rewarded by establishment of the diagnosis preoperatively.

Although all these cases of diastematomyelia were associated with occult spinal disorders in that no intraspinal contents were actually visible on the surface, in most of the

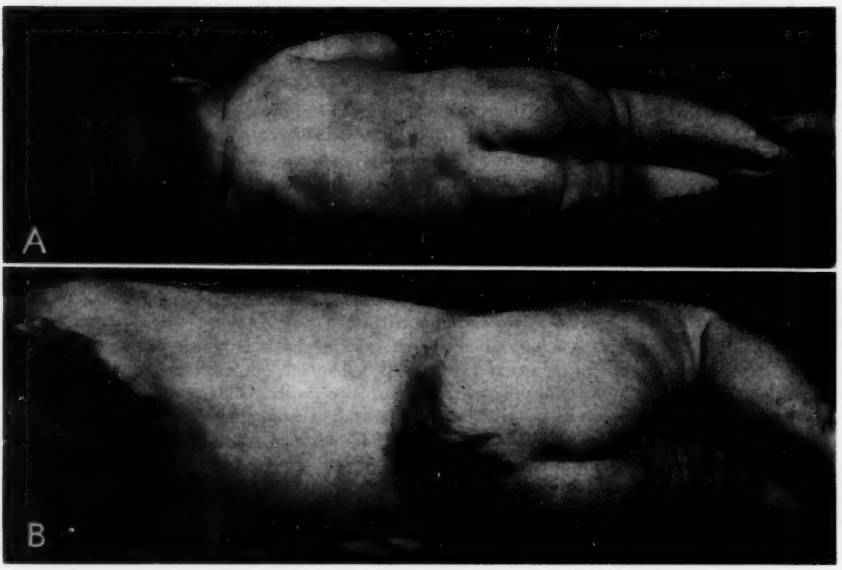

Fig. 1. A. Cutaneous angioma in lumbar region and midline sacral dimple in 4 mo. old girl (Case 9). Bony spicule at L_2 with division and fixation of spinal cord. B. Abnormal hair tuft in lumbar region in 8 wk. old girl (Case 5). Bony spicule at L_4 with division of cord and fixation of conus medullaris at S_1.

patients a cutaneous defect, usually in the midline, was present in the region of the underlying neural abnormality. The same variety of cutaneous defects were encountered as in other types of occult spinal disorders (Figs. 1 and 2). These consisted of abnormal tufts of hair (Cases No. 2, 5, 8, 9), skin dimples (Cases No. 3, 7, 9, 11), subcutaneous poorly circumscribed masses of fat (Cases No. 1, 10, 11) and port-wine stain or cutaneous angioma (Case No. 8).

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Sensory examination in this age group is difficult and unreliable and was rarely of help in this series. Urinary incontinence was the primary complaint in one patient (Case 1) and poor sphincter control was established on examination in four additional patients (Cases

6, 8, 9, 11). Unless there is complete incontinence, sphincter disturbances are not apt to become evident in early infancy, but later when toilet training should ordinarily be achieved. Regression in urinary control or reappearance of enuresis once it has stopped are especially significant.

Lumbar puncture findings are usually of no significance since this lesion does not cause a block to the circulation of subarachnoid fluid. A free flow of the opaque medium around the lesion was demonstrated fluoroscopically in the seven patients who had myelography performed. In the four patients with uncomplicated diastematomyelia in whom measurements were made, the total protein of the spinal fluid was normal in three and only slightly elevated in the fourth (55 mg. %).

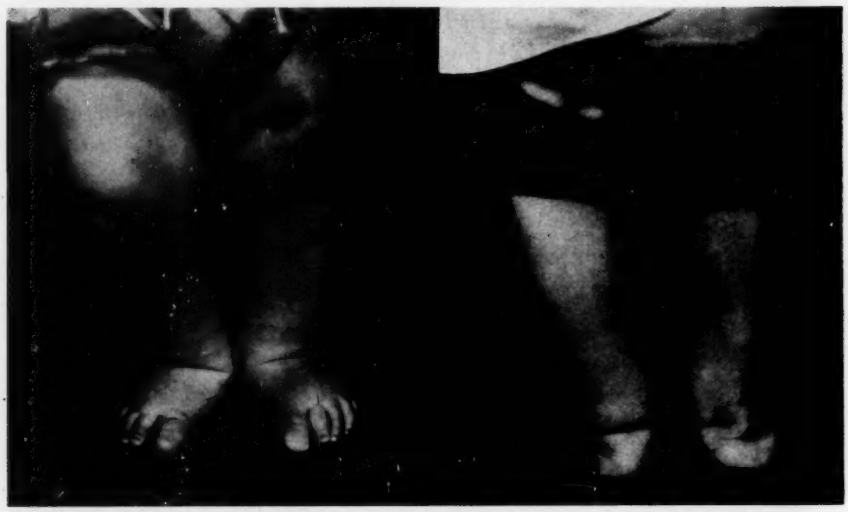


FIG. 3. Atrophy, shortening and weakness of left leg with bilateral calcaneo-valgus deformity of feet in 1 10/12 yr. old girl (Case 7). Bony spicule at T_{11} with complete division of spinal cord.

ROENTGEN FINDINGS

Roentgen diagnosis of diastematomyelia was made and later confirmed at operation in 8 of the 11 cases presented in this report. This lesion should be kept in mind when examining roentgenograms of the spine in orthopedic disorders of the lower extremities, undiagnosed disturbances of bladder and rectal function, or trophic skin disorders of the lower extremities. It is especially important to keep the lesion in mind when interpreting films which show a spina bifida occulta. Lateral films of the spine are usually of little help. However, antero-posterior films may show very clearly an abnormal line of increased density in the middle of the spinal canal (Fig. 6). It may sometimes be slightly eccentrically placed. It is usually in the area of other congenital anomalies of the spine, particularly defects in the spinous processes or laminae, but there may also be defects in the vertebral body at this level as well. There has usually been a fusiform widening of the spinal canal at the level of the diastematomyelia (Fig. 6). This widening of the canal may be several segments in length but is usually maximal at the level of the bony spicule. Narrowing of the pedicles and erosion of the posterior aspects of the vertebral

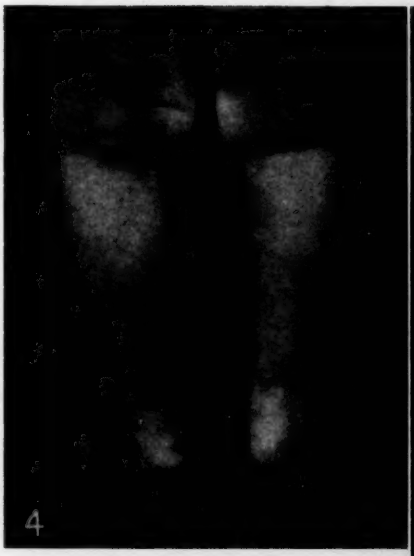


FIG. 4. Shortening, atrophy and weakness of right leg with absent ankle jerk in 1 6/12 yr. old girl (Case 3). Bony spicule at L_4 with complete separation of roots of cauda equina into 2 dural compartments.

FIG. 5. Deformity of toes of right foot associated with absent deep tendon reflexes in both lower extremities (Case 1). Bony spicule at T_{10} with asymmetric division of cord.

bodies, as seen with expanding lesions in the spinal canal, was not present in these cases.

Definite confirmation of the splitting of the dural canal may be obtained by myelography. This can be carried out satisfactorily at any age with "Pantopaque." Under the fluoroscope the opaque medium introduced into the spinal canal in an area away from the suspected lesion is seen to divide into two columns completely separated from one another and usually the opaque medium will outline the cleft in the intraspinal contents beautifully in spot films made during the course of the examination (Fig. 7). The exact level and extent of the diastematomyelia is then accurately recorded. Obviously this ex-

amination is of invaluable aid in planning and performing surgical exploration. A more detailed discussion of the roentgen evidence of diastematomyelia has been prepared for publication elsewhere.[9]

Surgical Treatment

The clinical importance of early diagnosis and treatment of diastematomyelia is based on appreciation of the relative anatomic changes which take place in the spinal axis as growth proceeds. After the third month of embryonic life the vertebral column and accompanying mesodermal structures grow at a more rapid rate than the spinal cord itself. Since the position of the spinal cord is fixed cranially because of its attachment to

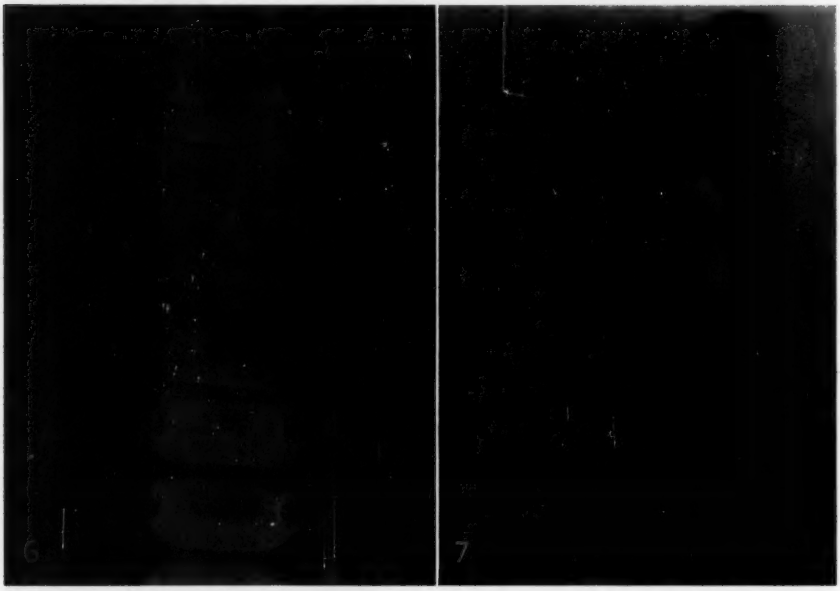


Fig. 6. Anterior-posterior roentgenogram of spine of 2 10/12 yr. old girl showing typical findings of diastematomyelia (Case 4). There is fusiform widening of spinal canal without compression of pedicles from T_6 through T_9. Midline bony spicule dividing cord is clearly visible at T_8.

Fig. 7. Spot-film made during "Pantopaque" myelography showing division of column of opaque medium at L_3 (Case 11). No bony spicule was visible in roentgenograms in this case but was found at operation to divide contents of canal completely into 2 dural channels.

the brain, the greatest changes in its relation to the vertebral column are seen caudally. As long as this differential rate of growth continues, the cord appears to migrate cranially and the more rapidly growing vertebrae necessarily shift caudally. Whereas the spinal cord and vertebral column are of equal length at the third month of embryonic life, by the time of birth the conus medullaris is found opposite the third or fourth lumber vertebra and by the time growth has ceased it lies opposite the first lumbar vertebra or slightly cranial to this point.

Normal neurologic function, particularly of the lower spinal cord and the cauda equina, depends upon the preservation of this differential rate of growth throughout infancy and childhood. If at birth or at any time in early life there is impairment of function due

to distortion or fixation of neural structures, then it is reasonable to expect that this loss of function will increase in severity if further growth results in a greater degree of distortion. It is important, therefore, at any time during infancy and childhood to remove, wherever possible, any obstruction to this normal "migration" of the cord in the spinal canal.

This may or may not result in improvement of any neurologic deficit present at the time of operation. The principle purpose, however, should always be regarded as a prophylactic rather than a curative one. The patient's parents should understand that surgical treatment is undertaken in order to permit normal growth and maturation of the nervous system and thus prevent, if possible, subsequent increase in loss of function. Repeated operative demonstration of distortion and fixation of the spinal cord by bony, cartilaginous or fibrous tissue septa through the spinal canal has convinced the authors of the importance of early surgical treatment.

Operation

Operative treatment in diastematomyelia is not particularly difficult and is carried out as any standard laminectomy. It has been performed in this series with the patient in the prone position under general intratracheal anesthesia. An exposure one or two segments above and below the site of the bony defect as visualized on plain roentgenograms or myelography is planned.

It is important to be extremely careful, as in all operations on spina bifida occulta, in approaching the spinal canal to avoid inadvertent damage to neural structures through an area of deficient bone. After removal of normal or abnormal spinous processes, laminectomy is usually best commenced at a level away from the lesion and then continued toward the abnormal area. It usually becomes evident immediately that the dural canal is widened in this region and, as the exposure is continued, the bony spicule protruding through the dura becomes apparent (Fig. 8). The spicule may or may not be attached to the under surface of the lamina at this level. There is often a defect in this lamina and spinous process so that the spicule is adherent only to fibrous tissue dorsally. Subperiosteal dissection down both sides of the bony spicule is carried out so that as much as possible can be removed before opening the dura (Fig. 9). This aids in protection of the spinal cord and also in the prevention of bleeding into the subarachnoid space. Bleeding from the spicule base is controlled with bone wax following which the dura is opened in the manner shown in figure 8. The dural opening is begun in the midline usually below the site of the bifurcation and carried around the edge of each dural channel adjacent to the spicule. The medial reflection of each dural canal is then removed. By freeing up numerous adhesions which are usually present between the spinal cord and the dura in this region, it is possible to retract each half of the cord in turn and continue excision of the bony spicule down to the level of the anterior dura. Arachnoidal adhesions are divided as far as necessary until the cord is freely movable. Usually it will be found that the two halves of the cord can then be approximated and will ride readily over the region of the previous fixation. No attempt is made to close the dura anteriorly. The dura posteriorly is closed in a linear manner, thus converting the two previous channels into a single dural canal. Routine wound closure in layers without drainage is carried out. It is needless to emphasize that as little manipulation of the spinal cord itself as possible should be performed. It is important rather to remove all structures which in any way distort the cord or prevent its free movement within the dural canal.

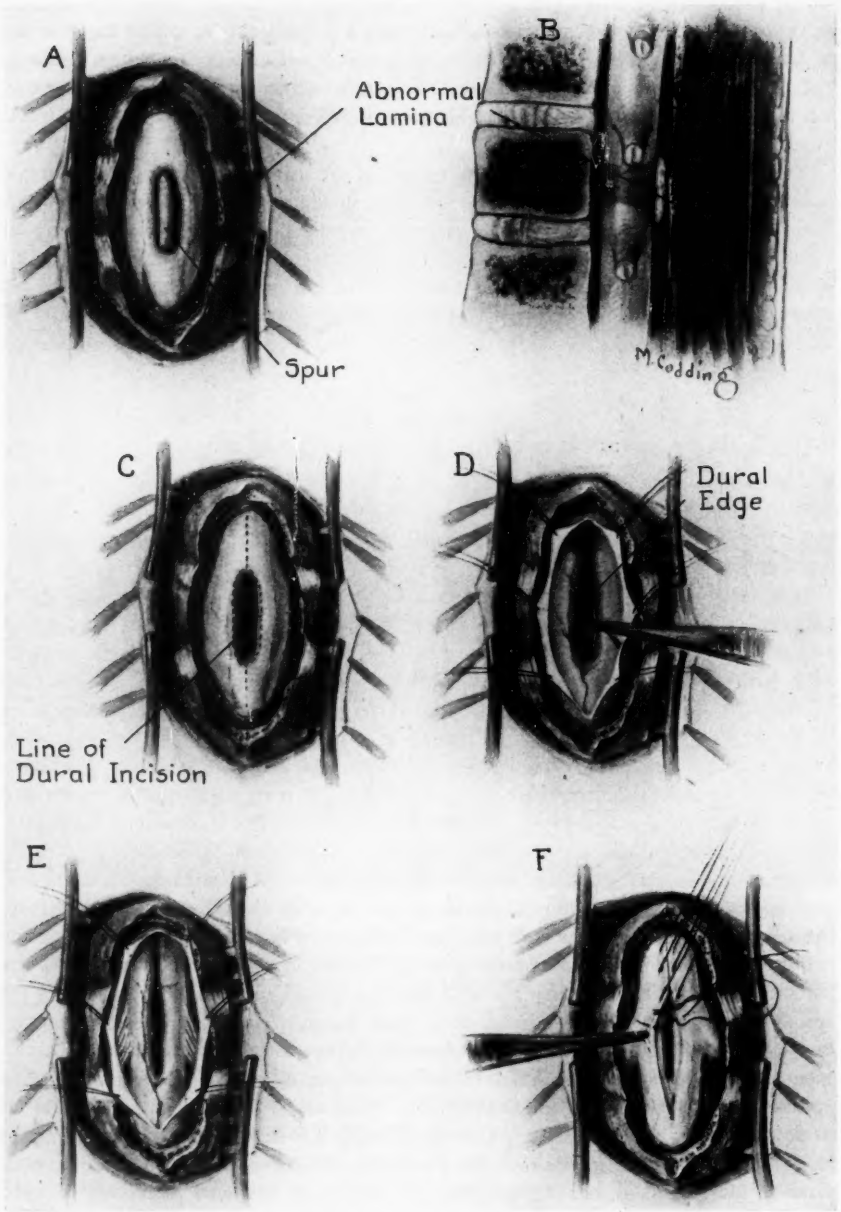


FIG. 8. A. Bony spur transfixing dura as exposed after laminectomy. B. Diagram of longitudinal section to show typical relations of bony spur. C. After extra-dural removal of most of bony septum divided dura is incised as indicated by dotted line. D. Arachnoidal adhesions to medial dural reflections are divided and excision of bony and dural septa completed. E. Separate halves of cord are now freely movable and approximate one another. F. No attempt is made to close dura anteriorly; posteriorly it is approximated in linear fashion. Routine wound closure in layers completes operation.

The operative procedure is essentially the same when carried out in the lumbar region for removal of septa transfixing the cauda equina. In this region it may be found that nerve roots have been diverted considerably away from their normal course and may be adherent to the septal structures. Division of the filum terminale, if this is adherent to a midline septum, is recommended.

Pathology

Since none of these patients died, there has been no opportunity to examine the distorted neural structures beyond the operative observations. In every case there was a bony spicule which completely separated the contents of the vertebral canal into two compartments. In all cases each half of the cord was invested by its own meninges. The size of the dural cleft approximated that of the bony spicule in every instance but the cleft in the spinal cord itself usually extended over several segments. It was common to find the division of the cord extending cranially as far as the bony exposure permitted observation but the two halves then reuniting immediately caudal to the spicule (Cases No. 5-8 and 10 and Fig. 10).

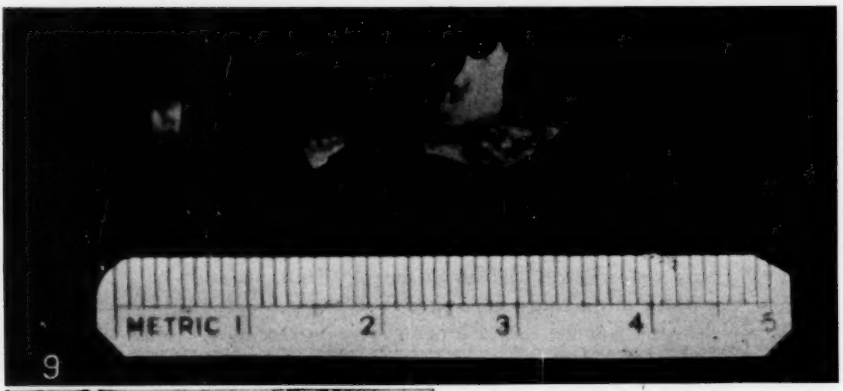
As far as could be ascertained by gross inspection, these cases represented division rather than reduplication of the spinal cord, that is, diastematomyelia rather than diplomyelia. The dura was opened in all but one patient, and the contents inspected directly. In only one patient did it appear as though any nerve roots emerged from the medial surface of either segment of the bifid cord (Case No. 1). In all the others in which the cord was divided (7 cases), normal appearing roots were seen to leave the lateral aspect of both halves of the cord and the medial aspects were entirely smooth and apparently covered with pia. There were usually numerous fine, presumably arachnoidal, adhesions between the medial surfaces of the bifid cord and the dural reflections investing the bony spicule. These were easily separated, ordinarily without danger to the cord. In three patients where the bony spicule was located at the fourth lumbar level, the cauda equina rather than the cord was separated into two compartments (Cases No. 2, 3, 11). In all these cases some of the roots of the cauda equina were adherent to the septum and were deflected considerably from their normal courses. These roots were apt to be smaller in caliber than normal.

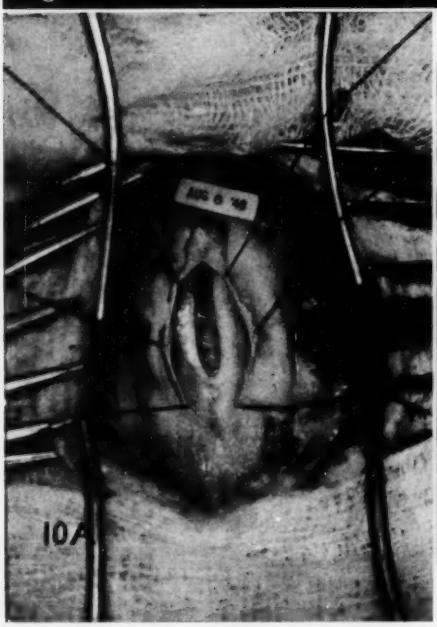
As noted in the summarizing table, the majority of these spicules occurred in the lumbar region. However, two were located at T_8, one at T_{10} and two at T_{11}. This is consistent with the relative distribution of other types of congenital spinal disorders.

None of these patients exhibited hydrocephalus or other clinical evidence of an Arnold-Chiari malformation. As stated elsewhere, they all showed some anomaly of the vertebral column in addition to the bony spicule. These anomalies included bifid spines, incomplete laminal arches, hemivertebrae, fused or small vertebral bodies, and widening of the interpedicular spaces. Two of the patients (Cases No. 6 and 9) had small dermoid inclusion cysts in the spinal canal at a level adjacent to the diastematomyelia.

Results

There has been no mortality in this group and no significant surgical complications. Postoperative reontgenograms have confirmed the removal of the bony spicule. In one patient (Case No. 4), who had shown rapid progression of spastic paraparesis during six weeks previous to laminectomy, a spicule at T_8 was only partially removed at the first operation. After this there were signs of increasing neurologic involvement of the lower





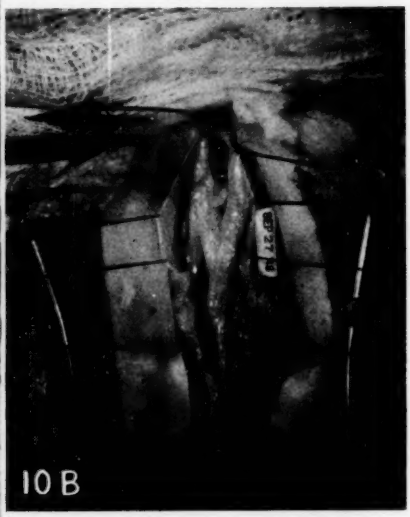


FIG. 9. Bony spicule removed in Case 4.

FIG. 10. Operative photographs after intradural exposure of divided spinal cord and removal of bony and dural septum. A. Case 8. B. Case 9.

extremities and sphincters. A more radical removal was carried out, facilitated by section of thoracic nerve roots, followed by immediate return of sphincter control and gradual improvement of voluntary motion in the lower extremities.

Only two of these cases (Cases No. 2 and 3) have been followed for more than 18 months. The early postoperative results have been encouraging. Six of the 11 patients have shown a definite improvement in the control of urination or in voluntary motion of the lower extremities (Cases No. 3, 7, 8, 9, 10, 11). In only the one case cited previously was there increase in neurologic impairment after operation and this was temporary. It

is again emphasized, however, that in general there is little improvement to be expected following this type of surgery and that such improvement should not be promised to the patient's family nor stressed to them as the reason why surgery should be performed. This should rather be regarded as prophylactic surgery. The purpose is to eliminate abnormal pressure on or distortion of the neural axis as completely as possible at any time during the growth period. It is the authors' definite conviction that progressive muscular weakness, increasing loss of sphincter control and progressive skeletal deformity can be slowed up if not completely stopped by removing any structures which transfix the spinal cord during early life and prevent its normal migration within the vertebral canal. If the cord and cauda equina are handled carefully at the time of operation, together with establishment of the supportive measures appropriate to major surgical procedures in young children, there is little risk involved and there may be much to be gained in the prevention of crippling disabilities.

Summary and Conclusions

Diastematomyelia associated with the presence of a bony spicule arising from the posterior aspect of a vertebral body and transfixing the spinal cord or cauda equina has been encountered in 11 operative cases. In the last nine of these the diagnosis was made previous to operation.

It seems apparent that progressive neurologic impairment of the lower extremities and of the rectal and vesical sphincters may result from increasing distortion of the neural axis as a result of fixation produced by these bony spicules during the growth period.

The diagnosis is suspected in the presence of cutaneous midline defects, muscular imbalance in the lower extremities, gait disturbances, deformities of the feet, urinary or fecal incontinence or increasing enuresis. The diagnosis is confirmed on roentgen examination by the presence of a midline opacity usually in the region of a spina bifida or other vertebral anomaly or by visualization of two separate subarachnoid channels on myelography.

Operative treatment consists in laminectomy with extradural removal of the bony spicule insofar as possible, followed by opening the dura with excision of its reflections adjacent to the spicule, excision of the remaining bony prominence down to the anterior dura, and division of all adhesions to the bifid cord or cauda equina until the latter is freely movable within a single dural canal.

In all these cases there appeared to be complete division of the cord or cauda equina into separate parts rather than reduplication of the cord. Each half of the neural axis was invested with its own meninges.

The operative findings in the 11 cases reported here, together with the brief follow-up observations noted to date, have convinced the authors that it constitutes good preventive medicine to carry out surgical treatment of diastematomyelia associated with spina bifida occulta at any time the diagnosis is made during infancy and early childhood.

Addendum

Since the preparation of this paper, three similar patients have been operated upon.

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SPANISH ABSTRACT

Diastematomielia (Fisuras Congénitas de la Médula Espinal); Diagnosis y Tratamiento Quirúrgico

Se ha encontrado la diastematomielia asociada con la presencia de una espícula ósea saliendo del aspecto posterior de un cuerpo vertebral y transpasando la médula espinal o cauda equina en 11 casos operativos. En los últimos nueve casos de éstos la diagnosis fué hecha antes de la operación.

Es aparente que el deterioro neurológico progresivo de las extremidades inferiores y los esfínteres rectales y vesicales puede resultar de la creciente torcedura del axis neural como un resultado de fijación producida por estas espículas óseas durante el período de desarrollo.

Se sospecha la diagnosis en la presencia de defectos de linea media cutáneos, desequilibrio muscular en las extremidades inferiores, desordenes en el porte, deformidades de los pies, incontinencia urinaria o fecal o enuresis creciente. La diagnosis se confirma en el examen de roentgen por la presencia de una opacidad de linea media usualmente en la región de una espina bífida u otra anomalía vertebral o por visualización de dos canales subaracnoideos separados en la mielografía.

El tratamiento operativo consiste en laminectomía con la eliminación extradural de la espícula ósea tanto como sea posible, seguido de la apertura de la duramadre con excisión de sus reflexiones adyacentes a la espícula, excisión de la prominencia ósea restante hasta la duramadre anterior, y división de todas las adhesiones a la médula bífida o cauda equina hasta que la última pueda moverse libremente dentro de un solo canal dural.

En todos estos casos parece haber completa división de la médula o cauda equina en partes separadas más bien que en reduplicidad de la médula. Cada mitad del axis neural fué revistida con sus propias meninges.

Los descubrimientos operativos en los 11 casos reportados aquí, junto con las observaciones breves hechas hasta la fecha, han convencido a los autores que constituye buena medicina preventiva para llevar a cabo el tratamiento quirurgico de la diastematomielia asociada con la espina bífida oculta a cualquier tiempo que la diagnosis se hace durante la infancia y niñez.

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TULAREMIA AS A PEDIATRIC PROBLEM

By HAROLD B. LEVY, M.D., CLARENCE H. WEBB, M.D., F.A.A.P., AND JACQUES D. WILKINSON, M.D.
Shreveport, La.

THE demonstrated efficacy of streptomycin therapy for tularemia imposes upon the practicing physician the obligation of early recognition of the disease in its varied forms. Toward this end a survey was made of all tularemia seen during the six year period 1943 to 1949 on the Pediatric Service of Shreveport Charity Hospital and in private practice (C.H.W.). This study of 48 consecutive cases shows considerable variation from the clinical picture presented in most pediatric texts and apparently justifies an altered concept of the problem which this disease presents in childhood.

HISTORICAL

Tularemia was first described by McCoy[1] in 1911 as a disease encountered among ground squirrels in Tulare County, Calif., whence he derived the name of the offending organism. Later, the human infection was given its name by Francis[2] who has added considerably to our knowledge of the disease.[3] Foshay[4] has contributed valuable researches in the preventive and therapeutic aspects.

Following initial studies in the West, tularemia was reported throughout the United States, ultimately in the New England area,[5] in all states except Vermont.[6] The indictment of numerous additional animal and insect vectors has converted the term "rabbit fever" into an archaic synonym. The importance of the tick has been demonstrated[7] and transmission by fish[8] and even by domestic animals[9,10] has occurred. Ingestion of infected material as a source of tularemia, especially in younger age groups,[11] and multiple sibling infection[12] are significant pediatric considerations. Primary lesions in the pharyngeal and tonsillar areas have been observed[13-16] as well as involvement of the central nervous system.[17] The role of increased awareness was illustrated by a recent report[18] in which the diagnosis was made accidentally by laboratory method. Unfortunately, no large series to date[19] has indicated incidence according to age groups and source or type of infection, other than a recent report from the Arkansas Board of Health.[20] Over a 10 year period in this state, 110 of a total of 704 cases were listed as occurring in the "pre-school and school child," ranking this group just beneath the agricultural worker and housewife in frequency of infection, emphasizing the importance of this disease as a pediatric problem.

SOURCE OF MATERIAL

The observations reported here result from a study of 48 unselected cases of tularemia in childhood seen during the past six years, two being from private practice and the remainder being encountered on the pediatric wards at Shreveport Charity Hospital. This institution is state-operated, drawing patients from the northwestern portion of Louisiana,

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with an average admission rate on the medical pediatric services of approximately 1200 infants and children annually, of which about 80% are Negro. During this same period, 121 cases of tularemia among adults were diagnosed in this institution.

Clinical Types

It has been customary to classify tularemia into four types according to the clinical picture: ulceroglandular, usually constituting 85 to 87% of reported cases; typhoidal, 8 to 10%; glandular, 3% and oculoglandular, 2%. This series indicates, however, that certain revisions in these concepts are necessary when dealing with tularemia in children (table 1).

TABLE 1

Clinical Types Among 48 Cases of Tularemia in Childhood

Ulceroglandular		21 cases (44%)
Pharyngo-Tonsillar		11 cases (23%)
Typhoidal		8 cases (17%)
Glandular		6 cases (12%)
Oculoglandular	*1 mixed*	2 cases (4%)

The comparatively large number of instances in which primary involvement occurred in the pharyngeal and tonsillar area requires the inclusion of a fifth and rather important type, which has been designated as "pharyngo-tonsillar." While the ulceroglandular form predominated with 21 cases, it constituted only 44% of the total, with the pharyngo-tonsillar group totaling 11 cases, or 23%. Typhoidal tularemia was seen in 8 instances (17%), glandular in 6 (12%) and oculoglandular in 2 (4%), one of which was combined with pharyngo-tonsillar involvement.

Sources of Infection

In 15 patients (31%), the tularemic infection was introduced through the ingestion

TABLE 2

Sources of Tularemic Infection

Ingestion (10 proved—5 probable)	15 cases 31%
Tick bite (11 proved—3 probable)	14 cases 29%
Animal contact	11 cases 23%
Uncertain	7 cases 15%
Mixed (ingestion and contact)	1 case 2%

of insufficiently cooked infected material, usually rabbit or squirrel. Tick bite was almost equally important, occurring 14 times (29%). Direct animal contact accounted for only 11 infections (23%), while the actual source was uncertain in 7 (15%). One child had both contact (oculoglandular) and ingestional (pharyngo-tonsillar) tularemia. (See table 2.)

Age Distribution

It may be of diagnostic significance to reclassify clinical groupings (chart 1) as they appear in the infant (0-2 years), preschool child (3-6 years) and school child (7-12 years). In the series reported here, the lone infection occurring under 2 years of age was typhoidal tularemia, while in the preschool group there were 5 instances each of

pharyngo-tonsillar and typhoidal forms, with only 4 of ulceroglandular and 3 in other classifications. In the older children there were 17 patients with typical ulceroglandular tularemia, only 6 with pharyngo-tonsillar, 2 typhoidal and 5 falling into other categories. Hence the older school child presents a picture more closely resembling that seen in adults; the younger child is more apt to have pharyngo-tonsillar and typhoidal forms.

Sources of infection follow a somewhat similar age pattern (chart 2), with the single

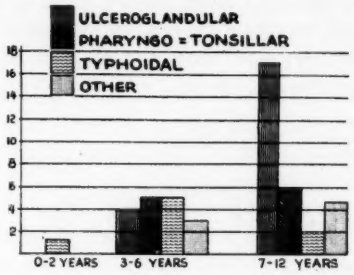

CHART 1. Clinical types of tularemia by age groups.

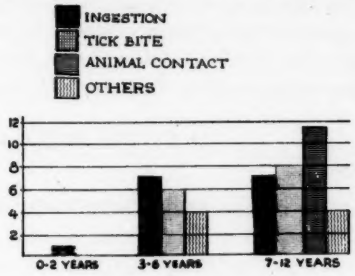

CHART 2. Sources of tularemic infection by age groups.

case in infancy attributable to ingestion, and the preschool children showing 7 infections from ingestion, 6 from tick bite and 4 from other sources. In the older age group, the adult configuration was more closely approached, with 11 cases from direct animal contact, 8 from tick bite, 7 from ingestion and 4 from other sources.

SEASONAL INCIDENCE

A further attempt was made to correlate the various sources with seasonal occurrence (chart 3). Ingestion was an outstanding source during the spring and summer months,

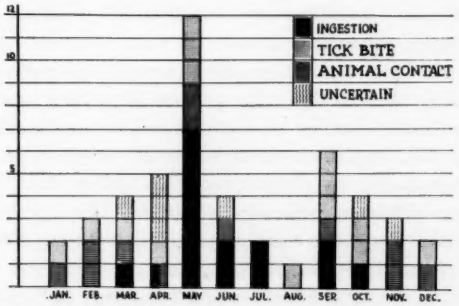

CHART 3. Incidence of tularemia by month of occurrence and source of infection.

with direct animal contact seen chiefly during the winter months. A comparable seasonal variation was reported in the Arkansas series.[20]

SEX AND RACE

The clinical types are correlated with race and sex in chart 4. The ulceroglandular and glandular forms occurred with overwhelming predominance in Negro males while the pharyngo-tonsillar type showed slight predilection for Negro females. The typhoidal and

oculoglandular types showed equal sex distribution. The occurrence of over 90% in Negro children is disproportionate to the usual ratio among hospital admissions and concurs with a previous report by Mathews[21] indicating increased susceptibility and morbidity in the Negro race.

Clinical Characteristics

Ulceroglandular: Ulceroglandular tularemia in this series differs little from the classical description of the disease as it appears in the adult, except for the fact that more than half the infections developed following tick bite, while only nine followed contact with rabbits and one with an infected squirrel. The combined animal sources, with one instance of

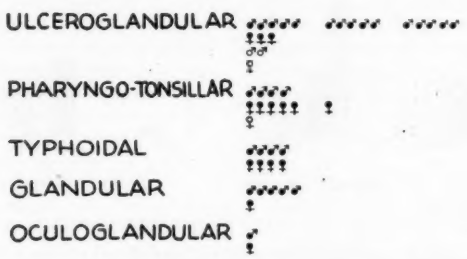

Chart 4. Clinical types of tularemia in 48 cases correlated with sex and race. Color of sex symbol indicates Negro or white patient.

tick bite on the elbow, made the extremities the most common location for the primary lesion; however, there were six cases, all due to tick bites, in which the initial site appeared on the genitalia. Other sites included the thoracic wall, neck and iliac crest. The complex of primary lesion with regional lymphadenopathy suggested the admitting diagnosis of ulceroglandular tularemia in 15 of the 21 cases of this type. Pyogenic infection was considered in four, while other conditions suggested included brucellosis, tuberculosis, typhus, acute disseminated lupus erythematosus and rheumatic fever. Further complicating the diagnostic picture was the presence of tularemic septicemia with pneumonic involvement in six patients. Fortunately, the first child survived with supportive care and specific therapy was available for the last five, so that no fatalities occurred in the ulceroglandular group.

Pharyngo-tonsillar: The importance of ingestion as a source of tularemic infection becomes apparent in reviewing the pharyngo-tonsillar group, since 9 of the 11 in this category gave a history of having eaten infected material. One case followed a tick bite on the neck and in the other the source was uncertain. Diagnosis was considerably more complex in this group, due to their resemblance to follicular tonsillitis, which was suspected in eight instances. Vincent's angina and typhoid fever were each considered three times, while the suggestion of diphtheria was sufficiently strong to justify administration of antitoxin in two. Tularemia was not considered in initial differential diagnosis and final evaluation was made only after careful questioning and clinical study. The description of a shaggy, necrotic exudate involving the pharyngo-tonsillar area, with marked cervical adenopathy, has been described by Anscheutz[15] and Waddell,[13] who also has called attention to the importance of sibling involvement in this type.[16] The majority of children in the present series who had pharyngo-tonsillar tularemia came from families wherein other members were infected. The first three patients seen were admitted with the father, who

later died of the disease. In the next case, the father had died of tularemia just prior to the child's admission to the hospital. Two others were siblings, admitted together and subsequently diagnosed as having pharyngo-tonsillar tularemia. Septicemic involvement occurred in 5 of the 11 cases, with one death, giving a mortality rate of 9% in the pharyngo-tonsillar group.

Typhoidal: Ingestion as a source of tularemia is again significant in the typhoidal form, as five of the eight cases acquired their disease in this manner. Two became infected from tick bites; in the remaining case the origin was obscure. Initial diagnostic considerations ranged from meningitis in three instances to brucellosis, rickettsial infection and even poisoning. Tularemia was thought of in the last two patients, as they were siblings admitted together. There were three other instances of sibling involvement in this group. Three of the eight children with typhoidal tularemia died (two within a few hours after admission).

Glandular: Cryptogenic infection was seen in six patients, only one of whom had a definite history of ingestion, the sources of infection for others being uncertain. Cervical adenopathy was outstanding in five patients; the sixth had pronounced axillary adenopathy. Tuberculosis was considered in four instances, pyogenic infection in three and Hodgkin's disease once. Only twice was tularemia thought to be likely on admission to the hospital. There were no fatalities in the glandular group.

Oculoglandular: This interesting form was observed in two cases, both following contact with diseased rabbits. Trauma to the eye was reported in the history of one, while the other resembled tuberculosis. This latter case also showed tonsillar involvement, giving a history of eating and handling presumably infected material. Both children recovered, even though the present therapeutic agents were not available.

Laboratory Diagnosis

The agglutination reaction, called by Foshay[22] "a test of amazing reliability," confirmed the diagnosis of tularemia in all instances, with exception of three fatal cases mentioned below and one other. However, this important test does not become useful until the 8th to 10th day of the disease, hence is of little diagnostic value in equivocal cases just when specific therapy is most urgent. To overcome this defect, Foshay[23] has developed an intradermal skin test which is reputedly positive in 92% of cases in the first week of disease. The requisite of species-specific serum and the unreliability of the commercially produced sera limit use of the skin test by the average practitioner. The skin test was not used in the present series. Blood cultures may be of assistance early, but technical difficulties and extreme dangers to laboratory workers[24] preclude widespread use of this means.

The appearance of numerous cross-agglutination phenomena added to the diagnostic difficulty. These included not only Brucella abortus and Proteus OX 19 as usually described, but also the heterophile antibodies.[25] A recent study[26] has shown that a number of conditions other than infectious mononucleosis may produce positive heterophile reactions, but to date the authors have found no mention of cross-agglutination with tularemia. A positive heterophile reaction was obtained uniformly in the 24 cases tested in the present series, the majority showing titers in excess of 1:112 or 1:224. The reaction was obtained as early as the sixth day of the disease, and showed gradual rise in many instances, in contrast with other cross-agglutination reactions which declined and then disappeared. This interesting observation is to be the subject of a later report.[27]

Therapy

Therapy with many agents in the preantibiotic era met with little success[28] until Foshay[4] developed a specific antiserum. Following Heilman's[29] demonstration of streptomycin effectiveness in experimental tularemia, evidence rapidly accumulated concerning its therapeutic value in human infection. A recent comparative study[30] indicates its superiority to immune and hyperimmune sera. Early reports of streptomycin therapy in children are by Cawley and Lafsky[31] for the ulceroglandular form and by Minden and Springer[32] in the oculoglandular type. Atabrine[33] and aureomycin[34–36] have been used, the latter apparently with considerable success although studies are still in the experimental stage.

Streptomycin has been available at the Shreveport Charity Hospital since late 1946. Thirty-two patients of the present series were admitted during this period; 24 received streptomycin therapy. Due to the limited supply and uncertainty as to dosage at the onset, there has been some irregularity in dosage schedules. The average total dosage used was 8.37 gm., given over an average period of 7.46 days. One child with pharyngo-tonsillar tularemia and septicemia received as much as 15.2 gm. within a nine day period; another

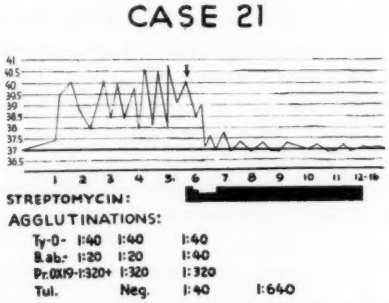

CHART 5. Patient L. K., showing temperature response to therapy and pertinent agglutination data.

with uncomplicated ulceroglandular infection required but 1 gm. daily for only four days. Even this amount may be in excess of actual requirements, since Foshay[37] recently indicates the optimal dosage as 0.5 gm. daily for two days, followed by 0.25 gm. daily for four days; or 0.5 gm. daily for six days.

Response was usually prompt and complete, with drop in temperature and amelioration of symptoms within 48 hours in practically every instance. The excellent results obtained can best be shown by two illustrative reports:

L. K., a 6 yr. old Negro boy, was admitted with his 3 yr. old sister, having a history of headache, loss of appetite, and listlessness for 2 days. His sister had similar but more severe symptoms and entered in a semicomatose condition. The uncertain history given by a relative afforded no evidence of animal contact or tick bite.

Physical examination revealed a lethargic Negro male who showed little of note other than generalized hyperactive reflexes with marked increase in hamstring tonus, slight tonsillar enlargement without exudate, and small cervical and inguinal lymph nodes. Temperature on admission was 37.5° C. Penicillin was begun with a dosage of 50,000 units initially, followed by 30,000 u. every 3 hr. However, the temperature rapidly rose to 39.5°, then 40° C., and assumed a septic pattern. Agglutination reactions were positive for Typhoid "O" in dilution of 1:40, Brucella abortus 1:20, Proteus OX 19 1:320 and Tularemia negative. Examination of the cerebrospinal fluid revealed no significant data. On the 3rd hospital day (6th day of disease) the clinical and agglutination pictures were essentially unchanged and cultures of the blood, stool and urine were reported negative. The patient's sister died

on the following day; autopsy findings showed extensive tularemic infection. On the same day the patient became lethargic and appeared to be seriously ill. Following discovery of tularemia in the sister, streptomycin was given in an initial dosage of 200 mg. followed by 100 mg. every 3 hr. for 8 doses, then 100 mg. every 4 hr. for 6 doses. There was an immediate dramatic response (chart 5), with return of the temperature to normal levels. As more of the agent became available, the streptomycin dosage was increased to 200 mg. every 3 hr. for 5 days, with clinical recovery following a total of 4.6 gm. The agglutination with B. Tularense became positive (1:40) on the 8th day, and by the 11th day had risen to 1:640. The further history was then obtained from another relative of frequent recent ingestion of rabbits and squirrels. This, together with the autopsy findings in the sibling, caused this case to be classified as one of ingestional typhoidal tularemia, successfully treated with streptomycin.

E. L. McG., a 3 yr. old Negro girl, was admitted with a history of high fever for 4 days, sore throat and swelling in the neck. She had been treated at home for presumed acute tonsillitis without improvement. The patient's mother stated that she had removed a tick from the child's neck several days earlier. Physical examination revealed an acutely ill Negro girl with a temperature of 40.5° C.; the pharynx was hyperemic and tonsils were large, with a shaggy necrotic exudate. The left postauricular and cervical lymph glands were enlarged. With persistence of a severely septic course after 36 hr. of penicillin therapy, the child was given a therapeutic trial with streptomycin, using 125 mg. intramuscularly every 3 hr. There was a rapid response (chart 6) with return of temperature to

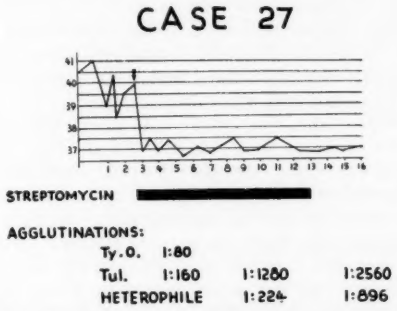

CHART 6. Patient E. L. McG., showing rapid fall in temperature after therapeutic trial with streptomycin, also data concerning agglutination reactions.

normal and general clinical improvement. Agglutination reactions on the day following institution of this therapeutic test were reported positive in dilutions of 1:80 for Typhoid "O" and Brucella abortus, and 1:160 for tularemia. By the 11th hospital day (15th day of disease) the agglutination titer against B. Tularense had risen to 1:1280, and the heterophile antibody titer was reported 2 days later to be 1:224; these 2 agglutinations later rose to 1:2560 and 1:896, respectively. Streptomycin therapy was continued for 10 days, giving a total dosage of 10 gm.

The first case illustrates the undoubted value of streptomycin when administered to a child who is severely ill with tularemia. The second case demonstrates additionally the value of a therapeutic test in equivocal situations, for a successful cure was initiated even before a definite diagnosis could be made by agglutination test. The results among 22 other cases treated with streptomycin were equally gratifying since all completely recovered, although 10 had septicemia. Early administration of the antibiotic probably did not interfere with development of natural resistance, as evidenced by later rise of agglutination titers in all cases regardless of the stage at which therapy was instituted. There were no evident instances of toxicity or sensitivity, and with the lower dosage now suggested there should be relatively little danger.

Mortality and Morbid Anatomy

There were four deaths among these 48 patients, but three of these occurred in the eight who had the dangerous typhoidal type of tularemia. The other death occurred in a patient who had pharyngo-tonsillar tularemia. Two of the patients died within six hours after admission. A brief summary of the fatal cases follows:*

L. M. H., a 4 yr. old Negro girl, was admitted with a history of anorexia, fever and sore throat for 4 days, and a profuse watery diarrhea for 48 hr. The child was in extremis on admission, with rapid thready pulse, shallow respiration and a temperature of 39.2°C. She died 1½ hr. later. Autopsy revealed many scattered small grayish-white tubercles in the lungs, liver, spleen and abdominal lymph nodes, along with extensive ulceration of the jejunum, ileum and ileo-cecal area. The microscopic features were compatible with tularemia, and animal inoculation with material taken from the spleen confirmed the diagnosis.

F. D., an 8 yr. old Negro girl, was admitted with a history of sore throat and fever for 3 days. Delirium developed on the day prior to entry. There had been no vomiting or diarrhea. Examination revealed a semicomatose child with irregular shallow respirations. Over the pharyngo-tonsillar area there was a yellowish-gray, shaggy exudative which could be easily removed; there was adjacent cervical lymphadenopathy. The child's temperature on admission was 40.8°C. Therapy with sulfathiazole and supportive measures was instituted and diphtheria antitoxin was administered on suspicion. On the 3rd hospital day, the additional history was obtained of ingestion of a rabbit that had been brought in by the family dog. Agglutinations for tularemia were negative on that day and the next, but had risen to 1:160 by the 13th day of illness. The patient died on the 14th day of her disease. Postmortem examination revealed tularemic involvement of the tongue, trachea, lungs, spleen, liver, stomach, ileum, kidneys, adrenals and abdominal lymph nodes.

P. M. K., a 3 yr. old Negro female, was admitted with her older brother, whose case was described elsewhere (v.s.) For the 2 previous days she had headache, anorexia, drowsiness, then vomiting and diarrhea. On the day before admission, the child developed nuchal rigidity and had a convulsion. Examination revealed an acutely ill child with muscle hypertonicity, nuchal rigidity and small lymph nodes in the axillary, cervical and inguinal areas. Temperature was 40.5°C. on admission. She was sent to the ward as "possible meningitis versus rickettsial disease." Spinal fluid examination revealed increased pressure, with 8 mononuclear cells, and normal levels for protein and sugar. Agglutinations on the 3rd hospital day were negative except for Proteus OX 19, which was positive in dilution of 1:160. A blood culture was reported to be negative. Under penicillin and supportive therapy, she continued to follow a septic course and died on the 5th hospital day, the 7th day of disease. Autopsy examination revealed extensive ulceration of the terminal ileum, cecum and ascending colon, with enlargement of the mesenteric and abdominal lymph nodes. Microscopic examination revealed tularemia of the ileum, colon, lungs, liver, spleen and lymph nodes.

J. M. C., a 14 mo. old Negro boy, was admitted with a history of fever and vomiting for 48 hr. Temperature was 40°C. on entry, and the child appeared moribund, with rapid and irregular respiratory efforts. Spinal fluid examination was normal. The patient died after 5½ hr. Postmortem examination revealed numerous irregular ulcerated lesions beginning in the first portion of the jejunum and extending throughout the entire small intestine. Microscopically, the lesions were typical of tularemia.

In these four cases, the location and extent of the lesions, predominantly in the small intestine, strongly indicate ingestional tularemia, although a definite history to support this could be obtained for only two. The second case showed characteristic clinical features of pharyngo-tonsillar tularemia, while the others were of the typhoidal type.

Summary

From the results obtained, it would appear that the lack of any pathognomonic clinical feature, tardy appearance of specific agglutinins, and variations from the typical adult

* Autopsies were performed by Dr. W. R. Mathews, Department of Pathology, Shreveport Charity Hospital.

course render imperative a high index of suspicion if an early diagnosis of tularemia is to be made in a child. Careful questioning concerning possible ingestion of infected meats, animal contact or tick bite must be stressed. Involvement of siblings may be a strong point in favor of ingestional tularemia.

Painstaking search for a local lesion should be made in every case with unexplained adenitis or appearance of sepsis; the frequency of pharyngo-tonsillar involvement must be appreciated. Usual laboratory aids may be of little value in early diagnosis in the average hospital or office at the present time. Early appearance of the heterophile cross-agglutination reaction may alert the observer to the possibility of tularemic infection.

A severely ill patient, for whom a definitive diagnosis cannot be reached, failing to respond to therapy for other suspected illnesses, and in whom any of the factors just mentioned prevail, should receive the benefit of a therapeutic test with streptomycin. Favorable response and survival, as is true of effective antibiotic therapy for other acute illnesses, may permit of later retrospective diagnosis in some whose illnesses or deaths would otherwise have remained unexplained.

Conclusions

Forty-eight cases of tularemia in childhood were observed over a six year period. Clinically, the inclusion of a new form, pharyngo-tonsillar, was prompted by the 11 patients (23%) who had involvement of this type. The typhoidal type occurred in 8 cases (17%), glandular in 6 (12%) and oculoglandular in 2 (4%). The typical ulceroglandular type, which predominates so overwhelmingly in adults, was seen in less than half (21 cases—44%), the majority of which occurred in older boys.

Ingestion of infected material and bite of the infected tick each accounted for nearly one third of the total infections. Direct animal contact, the usual adult source, was found in less than one fourth of the cases, all of these in older children. Infections resulting from ingestion and tick bite were seen chiefly during the summer months, those from animal contact during the winter.

A high index of suspicion is necessary if childhood tularemia is to be diagnosed early. The history must include careful questioning concerning tick bite, ingestion of, or contact with, diseased animals and possible involvement of siblings. Painstaking search for a local lesion, alertness to the possibility of pharyngo-tonsillar involvement, and suspicion because of unexplained adenitis or sepsis should prompt the examiner to consider tularemia.

Streptomycin has been used with striking success in treating 24 patients in this series, including 10 with tularemic septicemia. The effectiveness of streptomycin, together with the rapidity of response, has suggested a therapeutic trial as an important adjunct to early diagnosis. Any child who fails to respond to other medication, and in whom the possibility of tularemia is remotely suggested, should be given the benefit of streptomycin therapy, as the recommended dosage is sufficiently small to make toxic reactions unlikely.

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SPANISH ABSTRACT

Tularemia como un Problema Pediátrico

La tularemia de la niñez difiere de la enfermedad del adulto en la forma clínica y fuerte de infección. Un estudio de 48 casos mostró que menos de la mitad (21 casos—44%) fueron típicos ulceroglandulares, con una nueva forma faringe-tonsilar, designada a causa de 11 pacientes así clasificados. La tularemia tifoidal fué vista en ocho, la glandular en seis y la oculoglandular en dos. La ingestión del material infestado y las picadas de garrapatas fueron el resultado de una tercera parte de las infecciones totales, la primera es una fuente sobresaliente en los grupos de menos edad.

Complicación de "siblings" ("sibling"—uno o dos o más hijos de los mismos padres sin que necesariamente sean del mismo parto) fué un factor notable en la forma de ingestión. La ausencia de descubrimientos patognomónicos requiere un índice alto de sospecha para obtener temprana diagnosis, la que más tarde fué confirmada por reacción de aglutinación específica.

La estreptomicina es considerada actualmente el tratamiento de preferencia, se han obtenido excelentes resultados en 24 pacientes. Reportes de caso ilustrativos demuestran la respuesta rápida a este antibiótico. Con la dosis más baja que ahora se recomienda (0.5 gm. diarios por seis días), uno puede emplear con seguridad la estreptomicina como un ensayo terapéutico con mínimo peligro de efectos tóxicos y a menudo con resultados definitivos en casos equívocos.

1727 Line Avenue

HYPERCALCEMIA NEPHROPATHY AND ENCEPHALOPATHY FOLLOWING IMMOBILIZATION

Case Report

By KATHARINE DODD, M.D., HARRY GRAUBARTH, M.D., AND S. RAPOPORT, M.D., PH.D.
Cincinnati

WHEN a previously active individual becomes bedridden for a prolonged period of time many metabolic changes occur. Increased protein catabolism and associated disturbances in the metabolism of calcium and phosphorus may lead to osteoporosis, hypercalcemia and hypercalciuria.[1-4] War wounds, fractures and extensive paralysis caused by acute anterior poliomyelitis are circumstances leading to sudden immobilization of active individuals.

It has been hypothesized[1] that the skeletal structure during normal activity is subject to manifold stresses, hormonal and nutritional influences. The balance of these factors maintains a steady state between bone formation and destruction. With immobilization the equilibrium is upset, bone destruction exceeds formation and Ca is released into the extracellular fluid. The excess Ca is excreted mainly by way of the kidney. When the kidney is unable to excrete the increased quantity of Ca as rapidly as it is formed, renal damage and hypercalcemia result.

The urinary excretion of Ca increases during prolonged immobilization usually reaching a peak of approximately double the normal value one month following injury. The excretion remains high until the patient regains motion of his limbs.[4] During the early stages of immobilization the loss of Ca from the skeleton may not be apparent roentgenographically.

Albright and his co-workers[1] reported the case of an active 14 year old boy who developed osteoporosis with hypercalcemia after immobilization following a fracture of the right femur. Because of a persistently elevated serum Ca, a tentative diagnosis of hyperparathyroidism was made. Exploration of the neck region on two occasions failed to reveal a parathyroid adenoma. Following resumption of activity the osteoporosis and hypercalcemia disappeared with complete recovery of the patient.

The case to be presented is somewhat similar to the one reported by Albright et al.[1] It illustrates the importance of an understanding of the pathogenesis of acute hypercalcemic osteoporosis of immobilization which may occur in active children. The condition may easily be confused with primary renal disease, essential hypertension, intracranial disorders or hyperparathyroidism. Its occurrence is probably by no means as uncommon as the paucity of reports would indicate.

CASE REPORT

W. E., a 12 yr. old white boy admitted to the Children's Hospital, had always been active and well except for 2 attacks between the ages of 2½ and 3 yr., considered to be pyelonephritis, and an undiagnosed febrile illness at about 3 yr. of age. All his life he had voided once nightly.

The illness present on admission began 4 mo. before when he fractured his left leg while playing.

From the Children's Hospital Research Foundation and the Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati.

(Received for publication Nov. 13, 1949.)

The fracture was reduced and a cast applied. A few days later the patient began to vomit and to have severe headaches. Two months after the application of the cast, he had a generalized convulsion. Convulsive episodes continued off and on for 2 days. The cast was removed and the convulsions and vomiting ceased. Since the fracture was not healing properly, the boy was taken to a hospital 3 wk. later and the cast reapplied. Vomiting recurred and 10 days after admission he suffered another series of convulsions. Because of hypertension and papilledema he was sent to another hospital 5 days later for neurologic consultation. Ventriculograms were performed and appeared normal. A biopsy of the site of the old fracture revealed fibrous dysplasia with associated cyst formation. While in the hospital he was given large quantities of milk and sodium bicarbonate and received several blood transfusions. Serum Ca was 12.9 mg./100 cc. on the 8th hospital day and 14.6 mg./100 cc. 26 days later. Because of hypercalcemia, exploration of the neck for a parathyroid tumor was undertaken, but was without result since the parathyroid glands could not be identified. Hypertension, convulsions and hypercalcemia continued. Renal dysfunction became notable. NPN rose, hypertension was marked, the specific gravity of the urine was consistently low and repeated phenolsulfonthalein tests showed poor excretion of the dye. The boy was transferred to the Children's Hospital for further study and treatment.

Physical Examination

On admission at this hospital the boy appeared poorly nourished and irritable. The left leg was in a hip spica. Examination of the eye grounds revealed some blurring of both optic discs. The retinal vessels were not full but both old and new retinal hemorrhages were seen bilaterally. Blood pressure varied between 160 and 180 mm.Hg systolic and 120 and 130 mm.Hg diastolic.

The possibility was at once considered that complete immobilization had produced osteoporosis with hypercalcemia and consequent kidney damage and hypertensive encephalopathy. Previous renal damage as well as the high intake of milk and sodium bicarbonate might have aggravated the condition.

Laboratory Data

On admission the hemogram, except for a mild leukocytosis of 11.7 thousand/cmm. with a normal differential count, was within normal limits. The urine had a pH of 5.5, a specific gravity of 1.012, and contained a trace of albumin, some white and a few red blood cells. Urine culture revealed innumerable colonies of Esch. coli. Serum NPN was 45 mg./100 cc., pH 7.58, CO_2 32.7 and chloride 108.8 mEq./L., Ca 14.9 and P 3.7 mg./100 cc., phosphatase 4.9 Bodansky units, protein 8.9, albumin 5.5 and globulin 3.4 gm./100 cc.

RGs of the proximal end of the left femur taken through the cast revealed a partially healed fracture with some demineralization. They were suggestive of a pathologic fracture on the basis of a monostotic fibrous dysplasia. RGs of skull, chest and abdomen showed no abnormalities. The lack of enlargement of the cardiac shadow appeared incompatible with chronic hypertension.

Hospital Course

The early period of the boy's hospitalization was stormy. Shortly after admission he had 2 generalized convulsions 15 min. apart. Immediately following the 1st convulsion he lost contact with his environment and could not answer questions coherently. He cried, reached with his left hand for imaginary objects and was unable to move his right arm. During the 2nd day of hospitalization, he remained semistuporous and had intermittent convulsive movements. Tachycardia was noted. Breathing was shallow with a slow jerky component to each respiration. He vomited frequently. Throughout this period the boy was given continuous intravenous fluids for his dehydration and morphine for sedation and depression of his respirations.

By the 3rd day the convulsive movements had ceased but vomiting persisted. The next day the child became apprehensive, complained of hearing voices and of a thumping sound in the region of the left forehead. He began to scream and had severe convulsive movements of both upper extremities and of the face. Following the administration of sodium amytal the convulsions ceased, but the patient lapsed into a deep coma during which the respiratory rate varied between 5 and 8/min.

It was thought imperative to remove the cast and obtain greater movement of the extremities despite the roentgenographic evidence of incomplete healing of the fracture. The cast was removed 3 days after admission. Sulfadiazine therapy was started for the urinary tract infection. The symptoms of encephalopathy gradually decreased and convulsions became rarer and were confined to the right side of the body. By the 8th hospital day the child appeared aware of his environment, under-

stood conversations and was alert most of the time although he was suffering from occasional minor convulsions. No further convulsions occurred after the 11th hospital day. Intravenous fluids were discontinued and the boy was allowed to sit in a chair. A diet low in Ca was prescribed. Examination of the eye grounds revealed that the old retinal hemorrhages were fading rapidly. No new ones could be seen. The patient's condition continued to improve until the 22nd hospital day when he developed homologous serum hepatitis, thought to be due to a previous transfusion. The hepatitis gradually subsided. The anemia which developed following the hepatitis was treated by a blood transfusion and 1 mo. later the clinical condition had improved sufficiently for him to be up and

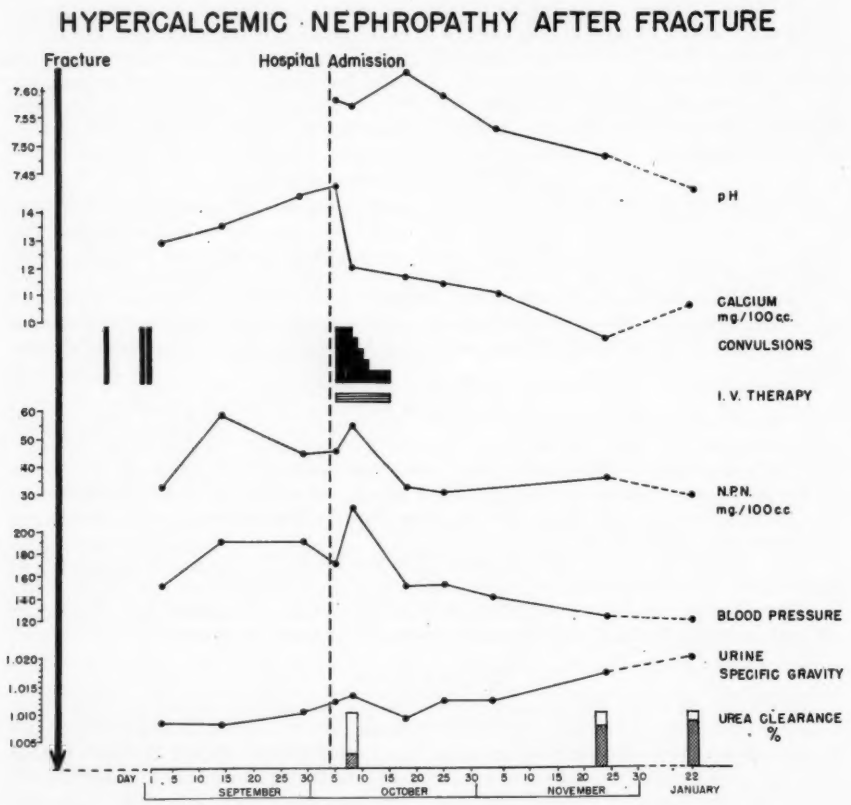

CHART 1. Course of nephropathy.

about. It was then noted that his left leg was approximately 2.5 cm. shorter than his right. He was permitted increasingly greater physical activity until discharge from the hospital 2 mo. after admission.

Albuminuria and pyuria were present to a varying extent the 1st mo. after admission. Thereafter the urine was essentially normal. Colon bacilli were cultured from the urine only on admission; later streptococcus fecalis and various other organisms were found after an in-dwelling catheter had been inserted. Bacteria could not be cultured from the urine after the 17th hospital day. The specific gravity of the urine, low at first, gradually increased to a value of 1.020 obtained during a concentration test 7½ wk. after admission. A urea clearance test performed 6 days after admission gave a value of 43.5% of average normal function. It rose to 80.8% of average normal function shortly

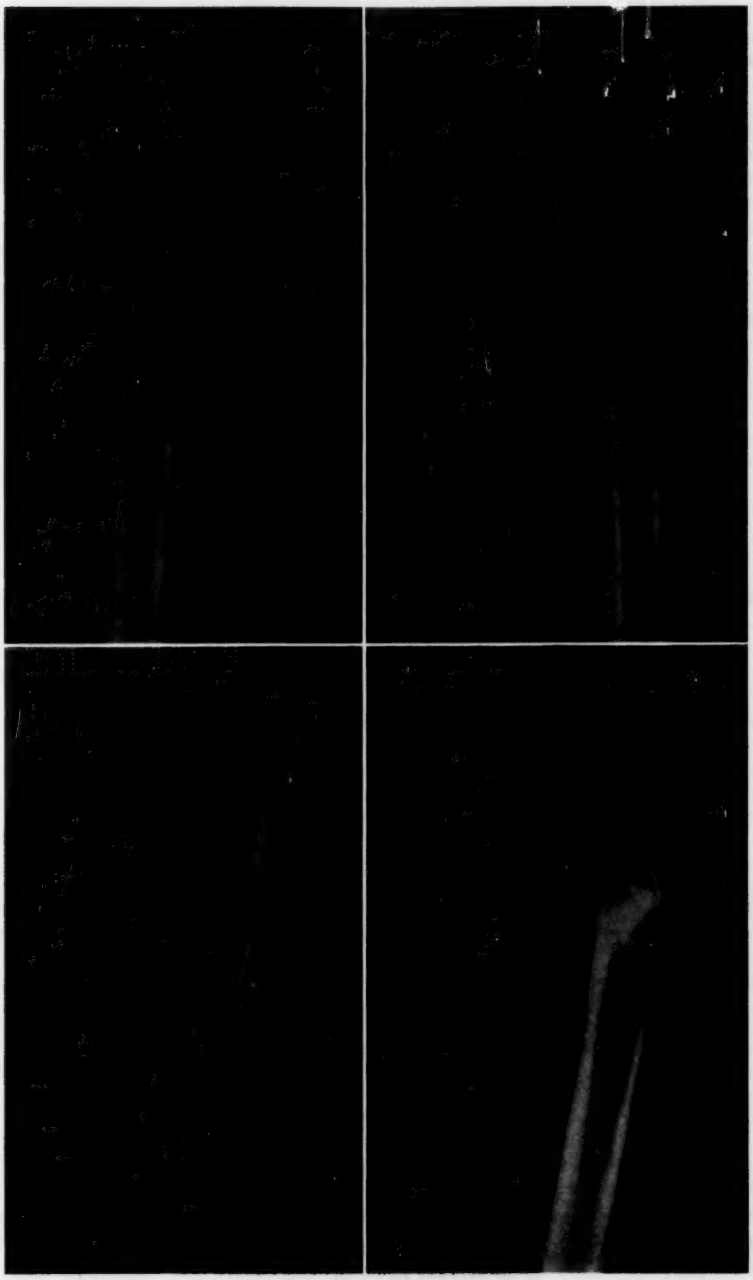

FIG. 1A-D. Roentgenograms of site of fracture.

before discharge. A phenolsulfonthalein test done late in the 2nd mo. showed 82% excretion of the dye at the end of 2 hr. Serum NPN rose from an initial value of 45 mg./100 cc. to 54 mg./100 cc. on the 4th day. Five days later it dropped to normal where it remained until discharge. Serum Ca decreased from 14.9 to 11 mg./100 cc. during the 1st 8 days of hospitalization and remained normal thereafter. The pH and CO_2 content were increased throughout the entire hospital stay, but tended to decrease as other functions improved. The blood pressure rose at first as symptoms of encephalopathy increased and fell rapidly as improvement in the patient's condition occurred. After 8½ wk. it had reached a value of 120 mm. systolic and 90 mm.Hg diastolic. The time course of these changes is represented in chart 1.

RGs of the left hip are shown in figure 1. The 1st film, A, taken 5 wk. before admission, demonstrates a healing fracture in the subtrochanteric area of the left femur. The bone proximal to the site of fracture is considerably demineralized and cystic rarefaction with irregular sclerosis is visible on either side of the fracture. Fairly good callus formation is present. The shaft of the femur distal to the site of fracture is normally mineralized. Film B taken in Cincinnati 3 days after admission shows, despite the presence of the cast, conclusive evidence of demineralization of the entire femur. This is manifested by coarsening of trabecular architecture. Confirmation of the demineralization is afforded by Film C, taken 1 mo. after admission, after the cast had been removed. Film D, taken 3 mo. after discharge, demonstrates progressive remineralization and healing at the site of fracture. Films of the axial and appendicular skeleton taken on the 15th and 42nd hospital days, respectively, demonstrated a generalized osteoporosis, coarsening of the trabecular architecture and exaggeration of the primary trabeculae at the ends of the shafts of the long bones.

These films may be interpreted as indicating a fracture in the subtrochanteric area of the left femur through an area of abnormal bone. Extensive demineralization of the entire skeleton followed probably as a result of immobilization. Following resumption of activity satisfactory remineralization of the entire skeleton took place and the fracture healed.

After discharge from the hospital the boy was allowed complete freedom of activity with the exception of running. He was asymptomatic until 18 days after discharge when he had a febrile illness and a short left-sided convulsion. He was readmitted to the Children's Hospital for further study 1 mo. later. Abnormal physical findings were limited to mild tenderness in the right costovertebral angle. His left leg was still thinner than the right. Hemogram was within normal limits. Blood pressure was 115 mm. systolic and 75 mm.Hg diastolic. Urine was normal. Its specific gravity varied between 1.012 and 1.020. Urine culture was negative. NPN was 29 and the urea nitrogen 14.9 mg./100 cc., pH 7.42, CO_2 content 25.2 and chloride 104.6 mEq./l., Ca 10.6 and P 4 mg./100 cc. of serum. The urea clearance showed 84% of average normal function. RGs revealed a healed fracture of the left femur and improvement in mineralization. Because of the recurrence of convulsions EEGs were done. The tracings were compatible with diffuse brain damage and a convulsive disorder. The abnormal waves were most marked in the leads from the left cerebral hemisphere. Anticonvulsant therapy was advised.

The boy was seen in the outpatient clinic 3 mo. after discharge. He appeared active and healthy, although he still walked with a slight limp. He was attending school regularly, was on unlimited activity and had gained 4.5 kg.

During the next 4 mo. he had 5 episodes of unconsciousness, the last of which was associated with a generalized tonic convulsion; otherwise he was asymptomatic. He was readmitted to the hospital 8 mo. after discharge at which time the laboratory studies revealed a normal urine with a specific gravity of 1.025 and a urea clearance of 100% of average normal function. After a short period of observation the boy was discharged on an increased dosage of anticonvulsant therapy.

Discussion

A consideration of the symptoms of the patient as they relate to his chemical disturbances is of great interest. Vomiting was the outstanding symptom during the early course of the illness. Headaches were a major complaint throughout. Vomiting also figured prominently among the symptoms of the patient of Albright.[1] Headaches associated with vomiting have been observed in patients receiving toxic amounts of vitamin D.[5] One may safely attribute these symptoms to hypercalcemia per se.[1, 6]

Several factors may be invoked in the genesis of the convulsions and encephalopathy. Hypertension was probably the major cause but an important role may be assigned to the impressive hyperventilation and metabolic alkalosis.[7] These factors combined to produce anoxia of the brain cells.[8] The hyperventilation responded temporarily to treatment with morphine but subsided only with general improvement of the patient.

The basis of the hypertension was the renal damage. It in turn was caused by the calciuria associated with the hypercalcemia.[1,4,6] Goormaghtigh and Handovsky[9] reported the occurrence of degenerative lesions in the arteriolar system of dogs suffering from hypercalcemia due to vitamin D intoxication. They pointed out that the vascular lesion was reversible as long as the smooth muscle cells of the artery had not reached the necrotic state. The severity of renal damage in the patient was clearly indicated by the persistently elevated NPN in the serum, the low specific gravity of the urine and the low urea clearance. His clinical course illustrates the reversibility of the renal damage.

One may speculate whether a pyelonephritis in early childhood constituted a subsidiary factor. It has been described that renal damage predisposes to metastic calcification of both vascular and tubular structures of the kidney.[6]

The transition of the patient from deepest coma through a stage of psychosis, neurotic disturbances and finally a condition approaching normalcy was of interest to watch. During the period of greatest hypertension and most severe convulsions, the boy lapsed into deep coma. As he improved he became disoriented as to time and place. He heard voices talking about killing someone and telling him dirty jokes. Periods of praying alternated with swearing. Euphoric episodes in which he called each nurse more beautiful than the last and wished to present his physicians with the whole state of Kentucky alternated with periods in which he was sure he was going to die and that everyone was treating him badly. With further improvement his sensorium cleared but he became a problem in management on the wards. He threw his food on the table, urinated at the table, hit the nurses, was flippant and resistive to all requests. Even these symptoms gradually improved until at the time of his last admission his behavior appeared practically normal. The presence of abnormal waves in the encephalogram and the persistence of convulsions when not under therapy indicate that there has been permanent damage to the brain cells.

Summary

The case of an active 12 year old boy who was suddenly immobilized following fracture of a femur is presented. The prolonged immobilization led to hypercalcemia and renal damage with hypertensive encephalopathy and osteoporosis. Following withdrawal of Ca from the diet, administration of intravenous fluids and increase in the child's activity, the serum Ca gradually returned to a normal level and signs of hypertensive encephalopathy and of renal damage disappeared. The pathogenesis of acute osteoporosis following sudden immobilization is briefly discussed.

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SPANISH ABSTRACT

Hipercalcemia Nefropatía y Encefalopatía Después de Inmovilización; Informe

Se presenta el caso de un muchacho de 12 años de edad quien fué repentinamente inmovilizado después de la fractura de un fémur. La prolongado inmovilización causó la hipercalcemia y daño renal con hipertensiva encefalopatía y osteoporosis. Después de la eliminación del calcio de la dieta, la administración de flúidos intravenosos y el aumento de la actividad del niño, el suero calcio regresó gradualmente a una cantidad normal y desaparecieron los signos de encefalopatía hipertensiva y el daño renal. Se trata en breve la patogenesis de la osteoporosis aguda después de la repentina inmovilización.

Elland and Bethesda Avenues

Pediatrics

VOLUME 6 JULY 1950 NUMBER 1

AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

REPORT OF THE EXECUTIVE BOARD MEETING

Philadelphia—March 28, 1950

A meeting of the Executive Board of the American Academy of Pediatrics was held at the Bellevue-Stratford Hotel, Philadelphia, March 28-29, 1950. The first session was called to order at 10 o'clock, Dr. Edward B. Shaw, President, presiding.

The following were present: Drs. Beaven, Grulee, Martmer, Bakwin, Barba, Bost, Kennedy, London, McElkenney, Stringfield and Wishropp.

Alternate District Chairmen present as guests and observers: Drs. Snedeker, Murray, McLendon, Hoyer and Overall.

The following applicants were approved for fellowships:

District I

Dr. Faith Newbury Ogden, Norwalk, Conn.
Dr. Joseph Osborne, Newton, Mass.
Dr. Frank Ashbrook Stewart, Newport, R. I.

District II

Dr. Charles Abler, Bronx, N. Y.
Dr. Stanford Borne, Valley Stream, L. I., N. Y.
Dr. Joseph Dolgin, Staten Island, N. Y.
Dr. John E. Gainor, Delmar, N. Y.
Dr. H. Louis George, Jr., Watertown, N. Y.
Dr. Martin H. Jacobs, Flushing, N. Y.
Dr. Nathan R. Kahn, Brooklyn
Dr. Joseph P. Michelson, Brooklyn
Dr. Arthur L. Ruby, Brooklyn
Dr. Bernard A. Schmierer, Brooklyn
Dr. Eli Yale Shorr, Brooklyn
Dr. Alex J. Steigman, New York City
Dr. Frederick H. Stiefel, Brooklyn
Dr. Frederick Lionel Tunick, Brooklyn
Dr. Samuel Untracht, New York City
Dr. Alfred Yankauer, Brooklyn

District III

Dr. David Baird Coursin, Lancaster, Pa.
Dr. Malvin Finkelstein, Jersey City, N. J.
Dr. Mervin Edward Fischman, Newark
Dr. Henry F. Lee, Philadelphia

Dr. Martha Frances Leonard, Highland Park, N. J.
Dr. Edward H. Meizlik, McKeesport, Pa.
Dr. Gerald J. Piserchia, Belleville, N. J.
Dr. Edward S. Szelewa, Newark

District IV
Dr. Dan P. Boyette, Kinston, N. C.
Dr. Lewis T. Corum, Tampa, Fla.
Dr. Marcus Emmett Farrell, Clarksburg, W. Va.
Dr. James Thomas Fowler, Jr., Chevy Chase, Md.
Dr. George Edward Prince, Gastonia, N. C.
Dr. Alexander J. Schaffer, Baltimore

District V
Dr. William Dwight DeVaux, Cincinnati
Dr. Ernest M. Eichhorn, Flint, Mich.
Dr. Martin Z. Kaplan, Louisville
Dr. John B. Larson, Louisville
Dr. Clarice L. McDougall, Grand Rapids
Dr. Robert P. Ostergard, Warren, Ohio
Dr. Carl L. Petersilge, Newark, Ohio
Dr. Frederick Adolphus Stine, Cincinnati
Dr. Ethon L. Stone, Jackson, Mich.
Dr. William Joseph Temple, Covington, Ky.

District VI
Dr. Walter M. Block, Cedar Rapids
Dr. Ronald N. Jefferson, Chicago
Dr. Beryl M. McDonald, Rockford, Ill.
Dr. Maya Strömberg Unna, LaGrange, Ill.

District VII
Dr. Milton Carl Bessire, Abilene, Tex.
Dr. Bruce Ward Everist, Jr., Ruston, La.
Dr. Gilbert B. Forbes, Webster Groves, Mo.
Dr. Julius M. Kantor, Kansas City, Mo.
Dr. Meyer Kurzner, Corpus Christi, Tex.
Dr. Bennett Joseph LaCour, Jr., Monroe, La.
Dr. Thurman Shuller, McAlester, Okla.
Dr. Fredric Elmer Simpson, San Angelo, Tex.
Dr. Don L. Thurston, St. Louis

District VIII
Dr. Oscar William Anderson, Seattle
Dr. Leroy O. Carlson, Walla Walla
Dr. John B. Castiglione, Visalia, Calif.
Dr. Robert F. Chinnock, Los Angeles
Dr. Nathaniel Gildersleeve, Pasadena
Dr. Esther S. Gross, Salt Lake City
Dr. Joseph Elbert Haddon, Bremerton, Wash.
Dr. J. Richard Hill, San Diego
Dr. Logan E. Jackson, Long Beach, Calif.
Dr. George Anderson Lamont, Vancouver, B. C.
Dr. Daniel A. Lagozzino, Everett, Wash.
Dr. Ben Mirman, Alhambra, Calif.
Dr. M. I. Vinnecour, Beverly Hills, Calif.

District IX
Argentina
Dr. Felipe de Filizalde, Buenos Aires

Cuba

Dr. José Manuel Mir y del Junco, Habana

México

Dr. Aurelio Gaytán Durón, Guadalajara
Dr. José Lavalle Peniche, Mérida, Yucatan
Dr. Ricardo Gonzáles Ruiz, México City
Dr. Alfredo Zepeda C., Guadalajara, Jal.
Dr. Carlos Avilés, Saltillo, Coah.
Dr. Gabriel Araujo Valdivia, México City
Dr. Julia Baker, México City
Dr. Lázaro Benavides, México City
Dr. Luis Berlanga Berumen, México City
Dr. Joaquín A. de la Torre, México City
Dr. Enrique Elizondo G., Durango
Dr. Andrés García R., Tampico, Tamps.
Dr. Jesús Gómez Pagola, México City
Dr. Armando G. Herrera, Chihuahua, Chih.
Dr. Jesús Ibarra Mazari, Puebla, Pue.
Dr. Fernando L. Madero, México City
Dr. Alfredo Madrigal Llorente, Torreon, Coah.
Dr. Pedro Daniel Martínez, México City
Dr. Francisco Padrón P., San Luis Potosi, S. L. P.
Dr. Alfonso Ruiz Escalona, Chihuahua, Chih.
Dr. Guillermo Siller, Monterrey, N. L.
Dr. Guillermo Zárate Mijangos, Oax. México City.

The following requests for Emeritus Fellowship were approved:

Dr. Albert J. Bell, Cincinnati
Dr. Gaylord W. Graves, Jackson Heights, N. Y.
Dr. Hyman Green, Boston
Dr. Harold L. Higgins, Newton, Mass.
Dr. William Merritt Taylor, Oklahoma City

The report of the Secretary was accepted as follows:

Since the meeting in San Francisco, the Secretary's office has been principally involved in clearing up the actions of the Executive Board at this meeting. There has been, of course, a great deal of work to be done on the Reorganization Committee and I am pleased to make the following report as to the vote, as of March 15, 1950:

"Yes" on both questions without comment	1,120
"Yes" on both questions with comment	73
"Yes" on No. 1; "No" on No. 2	59
"Yes" on No. 1 (No vote on No. 2)	18
"Yes" on No. 2 (No vote on No. 1)	5
"No" on No. 1	6
"No" on No 1; "Yes" on No. 2	13
"No" on both No. 1 and No. 2	22
Miscellaneous	3
Blank ballots returned	4
Total votes received:	1,323

Total affirmative votes on No. 1: 1,270.
Total affirmative votes on No. 2: 1,211.

The School Health Bill unfortunately passed the Senate in spite of the opposition to parts of it by Dr. Joseph S. Wall as representative of the Academy, but has not yet passed the House.

Dr. John P. Hubbard, Executive Director of the ICH Committee, resigned March 1, 1950, and Mrs. Elizabeth K. Lammie, Administrative Assistant of the Committee, resigned Feb. 15, 1950. Dr. Glidden L. Brooks has taken over the work of this Committee.

Since the meeting in November, there has been added to the funds of this Committee $2,000 from the New York Fund for Children, Inc., and $2,500 from the New York Foundation.

The Secretary attended a meeting of the heads of departments in the Central Region at the Palmer House on Feb. 5, which seemed to bring out a great deal of interest from the various men present.

The money from the Babe Ruth Foundation, which was appropriated for the use of the Tumor Registry Committee, has come through quarterly with regularity. The project of the Tumor Registry Committee has been approved by our Budget Committee and we are gradually getting the whole thing into shape. This will probably be a model upon which we can base any future contributions of a like nature.

The Academy has received from the M & R Dietetic Laboratories a sum of $2000 for a year's residency for a Latin American scholar, on solicitation by the Committee on Latin American Affairs.

It is now my sad duty to report the deaths which have occurred since my last report to you:

Dr. Stanley Brady, New York
Dr. Roy M. Greenthal, Milwaukee
Dr. Lawrence V. Hanlon, Brooklyn
Dr. Katherine M. Mayer, Chicago
Dr. Hugh Leslie Moore, Dallas
Dr. William Boyd Reading, Galveston
Dr. E. Warren Ripley, Montclair, N. J.
Dr. João Rodrigues de Souza, Recife, Pernambuco, Brasil
Dr. John A. Toomey, Cleveland (Past President)
Dr. Fessenden L. Day, South Chatham, N. H. (Emeritus Member)
Dr. Robert E. Ramsay, Pasadena (Emeritus Member)

Respectfully submitted,

CLIFFORD G. GRULEE, *Secretary*

The Treasurer's report was accepted as follows:

STATEMENT OF RECEIPTS AND DISBURSEMENTS

JULY 1, 1949 TO FEB. 28, 1950

Balance in checking a/c—July 1, 1949		$ 54,197.32
Balance in savings a/c—State Bank & Trust Company		24,252.31
Balance in savings a/c—First National Bank & Trust Co.		9,268.49
		$87,718.12
Receipts		
Dues	$69,192.92	
Exhibits—San Francisco, Nov., 1949	11,650.00	
Philadelphia, March, 1950	4,765.00	
Annual Meeting—San Francisco—Seminars	1,450.00	
Registration	4,853.00	
Round Tables	2,763.00	
Cash—Reg. Desk	4,787.50	
Areal Meeting—Philadelphia—Registration	2,283.00	
Initiation Fees	4,950.00	
Interest Earned	870.70	
American Cancer Society (For Tumor Registry)	5,000.00	
Committee—Improvement of Child Health	8,000.00	
Re-imbursement of $1,000.00 from Connecticut	1,000.00	
Pamphlets—Child Health Records $ 388.24		
Immunization Procedures 139.74		
Newborn Manual 1,097.50	1,625.48	
Certificate	1.00	
PEDIATRICS	24,475.00	
PEDIATRICS Special Account	11,736.61	
M & R Dietetic Labs, Inc.—Latin-Amer. Scholarship	2,000.00	161,403.21
		$249,121.33

Disbursements

Annual Meeting—San Francisco		26,819.42	
Areal Meeting—Philadelphia		480.51	
Bank Charge and Exchange		90.62	
Certificates		113.35	
Executive Board		9,021.97	
Miscellaneous		741.64	
Office Supplies and Equipment		498.61	
2nd Pan-American Congress		123.50	
PEDIATRICS		24,475.00	
Postage		1,015.35	
Rent		2,023.52	
Salaries—Secretary	12,000.00		
Assistant Secretary	3,333.32		
Executive Director, ICH Committee	5,000.00		
Office	7,844.73	28,178.05	
Stationery and Printing		1,006.43	
Telephone and Telegraph		509.15	
Travel—Secretary		704.74	
Treasurer's Bonds		302.50	
Expense—Districts	55.66		
States	111.55		
Committees	34,337.67	34,504.88	
Pamphlets—Child Health Records	39.25		
Immunization Procedures	16.20		
Newborn Manual	959.96	1,015.41	131,624.65
BALANCE—Feb. 28, 1950			$117,496.68
Balance in checking a/c—Feb. 28, 1950			64,611.95
Balance in savings a/c—State Bank & Trust Co.			29,329.24
Balance in savings a/c—First National Bank & Trust Co.			23,555.49
			$117,496.68

Respectfully submitted,

CLIFFORD G. GRULEE, *Treasurer*

Dr. Edgar E. Martmer presented a breakdown of the Treasurer's report into its various categories. He was thanked for the report and was asked to give a similar report, in mimeograph form, on the finances from July 1, 1949, to June 30, 1950, at the meeting of the Executive Board preceding the Annual Meeting in October and that this be presented to the State Chairmen at their meeting.

Dr. Martmer was authorized to complete the President's News Letter with a short résumé of the receipts and expenditures of the Academy.

Th report of District I was accepted as follows: "A meeting of the State Chairmen for District I was held in Boston on Feb. 26, 1950. Those present, besides the State Chairmen, were: the Alternate District Chairman, Dr. Lendon Snedeker, and, by invitation, Drs. Warren R. Sisson, Stewart Clifford and Ralph Ross.

The following activities of the Academy were discussed: reorganization; PEDIATRICS; pediatric education; the ICH Committee; centralization of the Academy's offices; qualifications and recommendations of a possible successor to Dr. Grulee. Much valuable information and guidance were obtained from this discussion.

Dr. James M. Baty was appointed Chairman of the State Chairmen to nominate the District Chairman to be my successor.

Child Care activities are getting under way in Massachusetts and Connecticut following their survey. Dr. Snedeker and Dr. Baty are doing an excellent job through cooperation with the State Medical Society.

Respectfully submitted,

OLIVER L. STRINGFIELD, *Chairman*

The report of District II was approved as follows:

The Upstate Chapter of New York State was formally organized at a meeting which was held in Rochester in October 1949. A constitution was drawn up and officers were elected. Dr. William J. Orr, Buffalo Upstate Chairman, President; Dr. Tyree Wyatt, Syracuse, Vice-President; Dr. Marjorie Murray, Albany, Secretary; Dr. Fred Bush, Rochester, Treasurer. Two areas of the Upstate Chapter, Rochester and Buffalo, are publishing reports on Child Health Care in their respective areas. The Buffalo report, which includes Western New York, has been published and distributed to all physicians, agencies and others who are interested in Child Care in Western New York.

A Child Health Committee has been established. Members of the committee are appointees from the Academy of Pediatrics, State and County Societies, the University of Buffalo Medical School, the Buffalo Children's Hospital, the Eighth District Dental Society, the Council of Social Agencies and several other organizations interested in Child Health.

The Buffalo Council of Social Agencies is serving as executive headquarters for the committee. In the published report, 15 recommendations were made regarding the improvement of child health care. Four of these recommendations are to be studied by the committee. These problems are: management and care of the premature infant; development of pediatric facilities in regional hospitals; post graduate education for the practicing physicians in this area; and an accident prevention program. An inaugural dinner will be held on March 20, 1950.

We take great pride and feel highly honored in the election of Dr. Paul W. Beaven of Rochester to the position of President-Elect of the Academy. We know he will do an excellent job for the Academy and wish him the best of success.

Section I and II of New York State (District II) met in September 1949 and voted on some of the matters at that time. No meeting has been held since then because the Academy itself did not see fit to honor our debt to the New York Academy of Medicine. Nevertheless, we expect to proceed this spring with organization.

Commissioner Mustard of the New York City Department of Health asked a group to be his Pediatric Advisory Committee for the years of 1948-1949 and many problems were discussed and procedures recommended for the New York Department of Health.

Dr. Thurman Givan reports that through local pediatric societies and sections many committees are working along the lines formulated by the Committee on Child Health.

One committee has set up a subcommittee to study the effect on infants born of mothers who had any virus disease during pregnancy. Each hospital has one member of the Academy assigned for this survey. Another committee is working to carry out the recommendations of the Academy's Committee on the Newborn.

Your State Co-Chairman is on the Pediatric Advisory Board of the Department of Health of New York City. This Board is at present cooperating with the Department in setting up centers throughout the city for the care of premature infants.

A general meeting has been arranged for April 1950 to discuss premature mortality and morbidity in the various hospitals of Brooklyn. Drs. Julius Hess and Leona Baumgartner will participate in the discussion.

The following are the results of the nomination for Upstate Chairman of New York, as of the afternoon of March 27:

Ballots sent	78
For Fred W. Bush, M.D.	44
For Tyree C. Wyatt, M.D.	1
Blank ballots	2
Ballots returned	47

Since 44 represents more than one half, Dr. Fred Bush is Upstate Chairman for New York.

Respectfully submitted,

HARRY BAKWIN, *Chairman*

The report of District III was approved as follows: Since the last meeting of the Board there is little new material to report. Each of the three states has held an official election just before or just after the November Board meeting, and the existing State Chairmen confirmed in their positions.

In Eastern Pennsylvania, Dr. Theodore Wilder was re-elected State Chairman; Dr. David Stewart Polk, Vice-Chairman, and Dr. George Clammer, Secretary-Treasurer. It is planned to develop a

Council of Fellows, consisting of members in strategic areas, who will guide the policy of the State Chapters. The Philadelphia group has been busy preparing for the Areal Meeting of March 30.

The New Jersey Chapter elected the officers nominated prior to the October 1 report from this District. The Chapter is continuing its activity in pediatric affairs throughout the state.

The District III resident rotation program is operating in a minor degree, but effectively. Two of the peripheral hospitals, Phoenixville Hospital and Montgomery Hospital at Norristown, Pa., have shared the services of a senior pediatric resident. Both hospitals have expressed themselves as delighted with the program. The residents employed have been pleased with the experience, and feel it has been time well spent. Further expansion of the plan will not be undertaken until present work is evaluated and careful groundwork explorations have been made.

Respectfully submitted,

PHILIP S. BARBA, *Chairman*

The report of District IV was accepted as follows:

A meeting was held in Winston-Salem on January 27 of pediatric educators from the Southeastern medical schools. This was well-attended and resolutions adopted urging the Academy to continue its efforts to improve pediatric education.

Respectfully submitted,

ARTHUR H. LONDON, JR., *Chairman*

The Chairman of District IV presented an additional report in the form of a letter from the State Chairman of the District of Columbia, Dr. Hugh J. Davis, requesting that Fellows of the American Academy of Pediatrics living in the metropolitan area of Washington but in Virginia or Maryland be permitted to be members of the District of Columbia Chapter of the Academy.

Dr. Davis' letter is to be taken up again at the fall meeting and fully discussed and the Secretary, in the meantime, is to communicate with the Washington group. A report is to be made at the State Chairmen's meeting in the fall.

The report of District V was approved as follows: Since the Annual Meeting the main activities in District V have been to continue or follow up the deficiencies as brought out by the survey made by the Academy under the direction of the ICH Committee.

Ontario has, of course, made no survey, but there was made a survey of the pediatric teaching in the Canadian medical schools and Dr. Silverthorne has submitted to the Central Office a complete résumé of this report.

Ohio has completed the organization of a state chapter and plans to hold a meeting bi-annually, one to be held in connection with the state medical society. This will improve and promote better liaison with the parent organization. This should result in carrying out the desires of the Academy in better dissemination of pediatric services and teaching. The program in pediatrics will be conducted at the state society meetings which will be of benefit to all concerned.

The Chapter has affirmed that along with local boards of health they would endeavor to improve the regular school health examinations made annually on Ohio school children. They would meet with various PTA groups, city and county health officers and improve this service by their own efforts. Such examinations should likely be referred to their private physicians and these should fill out the summer round-up forms in detail. They have suggested that, in cases where private physical examinations could not be afforded by parents, a clinic should be made available.

Dr. Nicholson, State Chairman from Kentucky, points out the many steps which have been taken under the auspices of the Academy in Kentucky since the Study on Child Health Services has been made.

Indiana has completed the organization of a State Chapter of the Academy and will have a meeting at least once each year, along with the State Society meeting and likely another meeting of its own at the time of the tri-state medical meeting held in either South Bend, Indianapolis or Toledo. Dr. Carlo as State Chairman has been both active and cooperative with the other Child Health groups in Indiana.

In Michigan there have been two meetings of the Academy Chapter, concomitant with the State Medical Society in Grand Rapids in the fall and a second in Detroit at the time of the Post Graduate Medical Institute. The members have been most cooperative in carrying out the school

examinations made annually on each child attending school and carrying out the immunization procedures recommended. Closer liaison with the State Medical Society, the Crippled Children's Society has been instigated, especially through the good work of our State Chairman, Dr. Van Schoick.

Respectfully submitted,

EDWARD A. WISHROPP, *Chairman*

The Chairman of District V read a letter received from the State Chairman of Michigan, Dr. Frank Van Schoick, describing the continuing development of Child Health Services in Michigan.

". . . Of all the services available to children of Michigan the one in most urgent need of expansion is that concerning mental health. Available child guidance clinics are too few and badly understaffed. The need for additional community responsibility and participation in the multitude of problems concerning child health is pressing. . . .

FRANK VAN SCHOICK, *State Chairman of Michigan*"

The report of District VI was accepted as follows:

Reports have been received from the chairmen of each state and province:

Illinois: The Illinois report of the ICH Committee will be presented in March to the Council of the Illinois State Medical Society for consideration and publication. This task was performed by Dr. McEnery and Dr. Poncher before Dr. Reichert became State Chairman for Illinois.

The program to improve the care of newborn and premature infants is progressing very satisfactorily, and the care of premature infants in Chicago, at least, is good. To secure a recognized pediatrician who would be in charge of each hospital nursery, the Committee on Fetus and Newborn has been working with the Chicago Health Department and the Maternal Welfare Committee. The hospitals in Chicago have been contacted but as yet only a few have expressed an opinion. It is apparent much ground work will have to be done to clarify the recommendation for the hospital staffs.

Not only Chicago but the entire state is aware of the need for a school health program and the present development of the Chicago School Health Program is arousing much discussion. In the near future, the local situation is expected to stabilize with the appointment of a Director of School Health for the Chicago Public School System. Once initiated, the state-wide program for the improvement of school health is expected to progress rapidly. It is anticipated that the aid of Dr. Hughes' Committee on Cooperation with the American Legion will be solicited although as yet the matter has not been presented to this Committee.

Iowa: The Iowa Pediatric Society will sponsor a speaker at the state medical meeting in Burlington, Iowa, on April 26, 1950. A day will be devoted to a program of pediatric subjects, which will include an address by Dr. Reynold A. Jensen. Fellows of the pediatric department of the University of Iowa will present 3 essays in competition for the annual award of the Iowa Pediatric Society.

Manitoba: Postgraduate teaching has been the center of activities. Preparations are being made for an extensive program of instruction in the care of newborn and premature infants. At the Children's Hospital on April 5, 1950, there will be a postgraduate program. Many rural general practitioners are expected to attend this meeting.

Routinely, all well-water samples which are submitted for analysis are examined for nitrate content.

To improve the care of newborn infants, the suggestions compiled by the Committee on Newborn Care are being translated into practical measures.

Minnesota: The Minnesota Chapter of the Academy was organized in August 1949.

The Minnesota Report of the Children Health Study, which is in the process of preparation, is expected to be ready in the very near future for the publishers.

Nebraska: The Nebraska Report of the Child Health Study has been completed and now is in the process of publication.

At the meeting of the Nebraska State Medical Society on May 3, 1950, the Nebraska Report of the Child Health Study will be presented briefly. Charts and maps will be prepared and will be exhibited in the section on scientific exhibits of the meeting.

A member of the Academy, Dr. Herman Jahr, has been appointed to serve on the Nebraska Committee of the Mid-Century White House Conference on Children and Youth.

During the past 3 months, 2 meetings of the members of the Academy in Nebraska have been held.

No action has been taken on the American Legion liaison although the matter has been discussed.

North Dakota: The North Dakota Pediatric Society which was formed last year held its first meeting of the year in conjunction with the meeting of the North Dakota Medical Society and will hold the second meeting in the fall. All the pediatricians in the state are members of the Society, and interested general practitioners are associate members. The membership of the Society numbers 30.

Saskatchewan: There is concern over the possibility of domination by the socialistic government of the Medical Council. Up to date this has been prevented. Because of popularity of hospital services which are free, the annual fee has been increased 100% and the physicians face some of the same problems that confront our British colleagues; namely, the high occupancy of hospital beds by aged and chronically ill patients in spite of fairly honest efforts on the part of physicians to avoid requesting admission for any but those in definite need of hospital care. This report reflects the opinion of physicians that they are in a difficult position whenever the patient insists upon admission to the hospital. The usual result is obtained; namely, there is difficulty in securing beds for patients suffering from surgical emergencies and many patients who are in need of surgery must wait many weeks to obtain admission to the hospital.

In the Province a program is developing for the care of crippled children, particularly those suffering from cerebral palsy.

South Dakota: The State Board of Medical Examiners is being urged to accord pediatrics greater recognition in the State Board examinations.

A member of the Academy has been appointed to serve on the South Dakota Committee of the Mid-Century White House Conference on Children and Youth.

Members of the Academy endeavor to impress upon the State Board of Health and the South Dakota Medical Society the existence of the American Academy of Pediatrics.

Wisconsin: Attempts are being made to secure the appointment of a pediatrician to the State Board of Medical Examiners.

Revision and improvement of the Department of Pediatrics in the local medical school is being carried out.

Arrangements are being made to establish a pediatric section in the Wisconsin State Medical Society, including separate officers and a delegate to the House of Delegates of the State Society.

Cooperation with lay organizations concerned with child welfare is being arranged. A member of the Academy, Dr. F. R. Janney, has been appointed to serve on the Committee of the Mid-Century White House Conference on Children and Youth. Pediatricians in the state work with the Wisconsin and National Association for Crippled Children and Adult. A cerebral palsy clinic for children will be established soon.

In various hospitals in Wisconsin, the recommendations concerning procedures in newborn and premature nurseries are being established.

Each member of the Academy in the state has been solicited concerning the ICH Committee and its continuation. The majority of the members favor termination of the Committee.

Respectfully submitted,

ROGER L. J. KENNEDY, *Chairman*

The report of District VII was approved as follows:

The membership of District VII has shown interest in the reorganization of the Academy.

Refresher courses have continued to be well attended in each state. General practitioners have shown interest in pediatrics by the attendance in these refresher courses and also in the establishment of more premature seminars.

The University of Arkansas has recently received a gift of a half million dollars to set up a children's ward in the proposed medical center. Arkansas has formed recently a pediatric society. There are 22 members. Much credit is due for this work in Arkansas to Dr. Francis C. Roberts, who is Medical Director of the Division of Maternal and Child Health.

The activities of the Academy have been definitely hampered by the action of the Louisiana Medical Society. Most of the state planning is done by the statewide medical council. Pediatrics has a very minority representation. Plans are being made for participation, however, in Louisiana with the American Legion, in their offer of assistance for pediatric education and for the formation of health councils.

The State Chairman of Kansas, recently elected, is Dr. Frank L. Menehan. Kansas members have been very active in their work on socialized medicine and have recently sent out a worker to try to stimulate interest in the rural area.

The Texas Chapter of the American Academy of Pediatrics was formed last November. Dr. John Glen was elected President.

Respectfully submitted,

THOMAS J. MCELHENNEY, *Chairman*

The report of District VIII was accepted as follows: 16 of the 17 members comprising the District Committee met in November in San Francisco at a luncheon. At that time we had a reaffirmation from all the State Chairmen that they were carrying on the activities as previously reported.

Respectfully submitted,

CRAWFORD BOST, *Chairman*

The report of District IX was approved as follows: The following plan of action for the Associate Chairmen (or Presidents) was formulated:

To make a pediatric census (survey) of the zones under the direction of the several Associate Directors, the latter asking for and making use of the collaboration of the Local (National) Directors of each of the nations included in their zone.

This census or survey is to cover the following points:

(a) The number of pediatricians with their corresponding addresses.

(b) The number of pediatric societies or children's welfare medical societies, including the number of members.

(c) The number and names of the educational or training centers (universities, hospitals or any other institutions in which pediatric education or training is offered either for doctors or nurses).

(d) Current pediatric literature (books written on this specialized branch of medicine, reviews, journals, etc., for doctors and for nurses as well). When this report is completed it will be the duty of the associate directors to send a list of books and new pediatric publications which may appear during their terms of office.

(e) The number of maternity and children's hospitals and institutions as well as other welfare institutions of a medico-social character (children's hospitals, pediatric services of general hospitals, maternity and children's dispensaries, public welfare or first aid stations with medical services —the latter donated by volunteer doctors not only at the stations but in hospitals, etc. Convalescent homes. A general report on the number of beds or consultations should be included for each of the institutions mentioned.

Be responsible for sending scientific papers or works for publication in PEDIATRICS.

Try to finance their own office.

Promote scientific meetings between the countries that make up each zone, preferably every 2 years, alternating with the Pan-American Congresses of Pediatrics.

To assume the responsibility of arranging for members of other countries the purchase of books and pediatric journals published in the Associate Director's zone. This is to be done through the aid of the Local (National) Director.

To support and aid in the activities of the Pan-American Congresses in a general way and especially by publicity of the said Congresses in each one of the countries included in the Associate Director's zone. This is to be done through the aid of the Local (National) Directors of each country.

General suggestions to be forwarded by the Regional Director (Chairman) of District IX to the proper authorities of the American Academy of Pediatrics.

1. That the General Director (Chairman) of District IX be included in the Editorial Board of PEDIATRICS.

2. That there be proposed the forming of a new zone with its corresponding Local Director for which post Dr. Germán Castillo of Nicaragua has been nominated, the said zone to include the countries of Nicaragua, Guatemala, El Salvador, Costa Rica, Panamá and México.

3. Because of the difficulties existing in some Latin American countries in the matter of obtaining

dollar exchange, to see about the possibility of some commercial firm (company), which may have representatives in the greater part of the Latin American countries, taking charge of making the payments in the United States of the dues and subscriptions of the members of the Academy so that the Office of the Affiliate of each country may receive the amount of such dues in the national money (currency) of its members.

Respectfully submitted,

FEDERICO GÓMEZ SANTOS, *Chairman*

The report from the Committee on Cooperation with Non-Medical Groups was accepted as follows: The committee has tried to set up certain standards of hygiene or health laws for various girls and boys in mixed camps over the United States. As usual it is quite difficult to get the state chairmen to appoint committees and, after doing so, it is hard to get an answer from them. It is planned now to work directly with the health officers in each state.

This has been done already with the state of Illinois and I find there are no definite health laws which control the health and hygiene of camps. We are going to find that is true with the other states also. After a statement has been obtained from each of the states we will then find out how we can attack such a problem.

If the Academy can get a seal of approval, either from the health departments of the state or from the Academy for each camp, it will be a valuable thing to parents and also to the owner of the camp as an advertising feature.

Respectfully submitted,

GERALD M. CLINE, *Chairman*

The following letter from the Committee on School Health was read, accepted and the recommendation contained therein approved: I wish to ask authorization from the Executive Board to include the American Association for Health, Physical Education and Recreation in the group with which we are negotiating a statement on desirable school health services. This latter association has asked to be included, and as they are a department of the National Education Association, I think it is wise for us to accept their offer.

In the January 1950 issue of the *American Journal of Public Health* there is a brief description of our informal collaboration with the American Public Health Association on School Health Service. I made this statement at the annual meeting of the American Public Health Association last October.

Respectfully submitted,

THOMAS E. SHAFFER, *Chairman*

The report of the Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases was accepted as follows: The Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases has been active through individual members. Criticisms and suggestions pertaining to the past editions of the book have been sought. Some members of the Academy, including Dr. Shaw, have been very helpful. There is a demand for brevity in recommendations and a deletion of reference to outdated therapeutic aids and procedures.

Respectfully submitted,

ARCHIBALD L. HOYNE, *Chairman*

A letter was read from the Committee on Mental Health and the Secretary was instructed to answer it saying, "This was contrary to policy; the Executive Board was not going to approve publication of anything over which it had no control as to subject matter or distribution." The National Mental Health Foundation of Philadelphia is a reliable agency concerned in promoting mental health of the American people. The president is former Justice Owen J. Roberts. Dr. Fred H. Allen is on the Board of Trustees which, for the most part, consist of well known persons. One of the executives of the Foundation asked me to try to get Mead Johnson or other corporations to furnish funds for printing a pamphlet on "Behavior Problems of Children," which was prepared by the National Committee on Mental Hygiene. The pamphlets so printed are to be distributed gratis to the members of the Academy of Pediatrics.

I told the foundation I could not go to anyone for such funds unless I had the approval of the

Executive Board of the Academy. However, I said I would send this letter to you for opinion. I would appreciate such when you and the other members are able to pass on the matter.

Respectfully submitted,

MILTON J. E. SENN, *Chairman*

The report of the Committee on Latin American Affairs was accepted as follows: Since the meeting in San Francisco, the Committee has interested itself in attempting to obtain funds for scholarships for Latin American pediatricians to study in this country. The advances have been made to only commercial firms and, at the present time, one of them, namely, M & R Dietetic Laboratories, has given $2000 for a scholarship. The proposition has been turned down by 2 or 3 of the companies but several others are considering it and it may be that we will have from 3 to 5 scholarships from these sources.

It is altogether likely that we will have difficulty contacting foundations who are interested in this objective because most of them have their own programs of a like nature. However, at the present time, we have made a start and we hope in the near future it will be possible to increase the number of scholarships.

We are attempting to revamp the system of appointments and also to make some definite rules regarding the training to be had in this country.

Respectfully submitted,

CLIFFORD G. GRULEE, *Chairman*

The following letter from the Committee on Pediatric Awards was read and accepted:

Although nominations have been received from 6 out of 7 members of the Committee, suggestions are so discordant that I doubt it will be possible to make the final acception of recipients until we get together probably at the meeting of the American Pediatric Society at French Lick.

Respectfully submitted,

DONOVAN J. MCCUNE, *Chairman*

To start the Program Committee report, a letter from Dr. Esther Clark was read as follows: "I note with some distress that the American Academy of Pediatrics has made no official recognition of the fact that more children die of accidents, by far, than from any other combined causes. I feel that anything at all that causes death and disability is the business of doctors, even though it is something that can't be investigated by laboratory or medical means. Hence I feel that it is extremely desirable that either a committee be formed to see what can be done to further the prevention of accidents in children or that the situation at least be given a very strong official recognition by the Academy.

"Many lay organizations are well aware of this and the National Safety Council, of course, is doing a tremendous amount of work along this line. The Metropolitan Life Insurance Company is also giving a good deal of publicity to this matter. I feel that we are perhaps lagging a little bit in not being leaders in this matter. It seems to me not at all illogical even to set up a National Foundation for the Study of Accident Prevention and see that real scientific investigation methods are applied and see what may be done to reduce both the mortality and morbidity of accidents among children."

This matter was referred to Dr. George M. Wheatley for advice.

The Report of the Program Committee and recommendations were accepted.

The Report of the Committee on Care of European Children was accepted as follows: We are continuing our activities in connection with the Committee on the Care of European Children. Small groups of children are being admitted to the Reception Center and medical care has been amply provided.

Respectfully submitted,

CARL H. SMITH, *Chairman*

The Report of the Committee to Cooperate with the United States Food and Drug Administration was accepted as follows: There have been several requests from Dr. Kerlan of the Food and Drug Administration for assistance. These have been handled either by correspondence with members of

the Committee or with other specialists who were in a position to give authoritative answers to the questions asked.

Respectfully submitted,

WALDO E. NELSON, *Chairman*

The following letter from Dr. Harold K. Faber was read: "At the next meeting of the Executive Committee of the Academy of Pediatrics, I suggest that the Committee give consideration to the desirability of setting up a new subcommittee to study the problem of drug dosage in infants and children. Standards now in general use such as Clark's rule and Young's rule are unsatisfactory, especially for infants, and pediatricians tend to use empiric dosages based largely on individual experience. Some recent attempts to base dosage on surface area would appear to have the advantage of being relative to metabolism rather than weight. As an example, for an infant of average size at the age of 6 months, the dose of a given drug by weight would be about ⅛ of the adult dose; by Young's rule, 1/25, and by surface area, about 1/5. On the basis of personal experience, I should suspect that the last of these is more nearly correct than the other 2. It may be that still another point of reference may be better. In any case, I believe that the subject is one of prime importance, and deserves careful study by the Academy in collaboration perhaps with pharmacologists."

The Executive Board voted to appoint Dr. Faber Chairman of a Committee to be appointed by him to carry through on the information contained in his letter.

The Report of the Committee on Surgery was accepted and contents noted as follows: The possibility of admitting to the section men who are doing less than 90% of children's surgery occasionally arises, but there is no disposition on the part of the committee to reduce the percentage at the present time. We are, however, keeping a file of the men who are doing a large percentage of children's surgery in their districts for references and perhaps contact in the future.

Co-operation between the section and the Program Committees has been discussed. We are thinking of a session of the Surgical Section at the Chicago meeting for discussion of interesting surgical subjects, at which, of course, all members of the Academy will be welcome.

There seems to be a possibility of an increase of the Surgical Section from the South American cities.

Respectfully submitted,

HERBERT E. COE, *Chairman*

The following letter from Dr. Bret Ratner was read: ". . . The question of importance is whether the members of the Allergy Section can participate with the Board of Pediatrics in relation to examination for some subject certification in allergy. If this linkage could be established, it would help greatly in getting the proper type of trained men for future members of the Allergy Section. This question has been discussed by the Board of Pediatrics. I should also like to propose that a panel on the question of allergy and childhood might be a good subject for a Pediatric Section to plan to give at our next meeting. If this meets with the approval of the Program Committee, I shall proceed to arrange for it."

The Executive Board took the following action on the above letter: "Moved that they felt the question of the development of the fellow in allergy and pediatric allergy is a matter for the Board to decide and not for the Academy"; they also "Moved that the Program Committee be empowered to consult with any component group, but are not necessarily bound by their suggestions."

The Report of the Committee on Publicity and Public Relations was accepted as follows:

There continues to be more than the usual interest in Academy affairs. Many of the fellows ask for information and I actually had a letter from one of the fellows in my district commenting on the policy of the Academy for the future National meetings.

Mr. Lawrence Selz has taken a personal and active interest in the Publicity program of the San Francisco meeting and the Eastern area meeting to be held in Philadelphia.

The American Legion has been holding area meetings, several of which have been attended by Academy members, and they're interested in having that cooperation from the national groups in their plans on Child Welfare.

Respectfully submitted,

PHILIP S. BARBA, *Chairman*

A report from the Committee on Pensions and Annuities was presented and accepted as an interim report and the Committee instructed to proceed further with the investigation and bring in a definite recommendation at the time we have a reorganization.

Dr. Harold D. Dargeon was present and presented the following report for the Committee on Tumor Registry: The following changes in the membership are recommended: Dr. Alfred J. Vignec, 39 A Grammercy Park, New York City, and Dr. John E. Franklin, 56 East 76th Street, New York City, as additional members of the Committee. Dr. Hayes E. Martin, as you know, has been a member of the Committee since its organization, although he is not a member of the Academy. His interest and cooperation have been of great help to us. I would like to recommend that his position in the Committee be changed to that of consultant.

Respectfully submitted,

HAROLD W. DARGEON, *Chairman*

The Executive Board moved to approve the membership of the Committee.

Dr. Dargeon presented a letter from the Loyal League Philanthropies, Inc., re a grant of $4,000 for a research project of the Committee for the Study of Radiation Effects in Childhood. The Executive Board moved to accept this fund in the name of the Academy, to be dispensed by the Academy through the Tumor Registry Committee in the same manner that the Babe Ruth Fund is.

The Executive Board moved that the Secretary be empowered to solicit funds from the Babe Ruth Foundation in the name of the Academy for the Committee on Tumor Registry.

The Report of the Committee to Investigate Activities and Personnel of Tumor Registry Committee was presented by Dr. Stringfield as follows:

We would like to recommend that the consultation service which at the present time is located in New York be established throughout the country and that the members of the Academy and the profession as a whole have access to it.

Information relative to this consultation service should be sent to the Director of Pediatrics at the various hospitals throughout the country, with a note that this information is to be filed in the hospitals, so the members of the profession, general practitioners, surgeons and so forth, would have this information available as to where they could get consultation service, both from the diagnostic standpoint and otherwise.

The committee might prepare a small primer relative to pertinent diagnosis of these various neoplastic conditions which arise. That can be done very easily.

The committee of consultants, at the present time, are all pathologists, and it is suggested that if consultation groups are established throughout the country, members in the field of radiology, dermatology and surgery should be included, this work being done more or less as subcommittees instead of making it the main committee. The point about the subcommittees through the country was broached several years ago and it is wondered whether it would be well to have areas, possibly connected with our district areas, which might serve as central bureaus for aid in diagnosis and consultation under the main committee or whether this might be done in conjunction with the surgical associates of the Academy.

It was voted to accept the Report of the Committee to Investigate Activities and Personnel of Tumor Registry.

The pamphlet, "Childhood and Cancer," was presented by Dr. Dargeon and discussed. The Board voted to have this material submitted to them in mimeographed form for their individual expression of correction, approval or rejection, and then acted upon at a later time.

The Report of the Liaison Committee with American Medical Association was accepted as follows: A meeting of the American Academy of Pediatrics and the American Medical Association Liaison Committees was held in Washington, D. C., on Dec. 6, 1949. Present were Drs. Weston, Crawford and Barba for the Academy; Drs. Martin, Wall and Nicholson for the AMA. The Academy Committee reported on actions taken by the Executive Board as follows:

1. The Executive Board of the Academy, while realizing that the Academy was the only national medical organization interested solely in Child Health in all its phases, also realized that the practical application of developments in that field could only be accomplished to the fullest extent by close cooperation with the AMA and its component units.

2. In regard to matters of policy and of legislation the feeling was that being a national group and a separate organization, the Academy should express its opinion on such matters. The sentiment

of the Academy would in practically all cases parallel that of the AMA in regard to matters of compulsory health insurance and socialized medicine in general.

3. The Board and most of the membership are aware of the AMA plans to raise an annual fund for medical education and will be glad to cooperate with them and help further such a program in which we all have a vital interest.

4. Dr. Anderson has notified the Board that the Council on Education and Hospitals will welcome cooperation with our Committee on Education. The Board authorized payment of expenses for a member of our committee to attend any meeting of the Council when joint action was desired.

5. Dr. Thomas E. Shaffer's report of our Committee on School Health was forwarded to the joint committee. In this report he has recommended that there be drawn up a declaration of desirable practices and standards which would apply to any situation in school health under federal, state or community sponsorship. His committee has been working with other national groups endeavoring to set up such a declaration. He points out that passage of the bill in the Senate was accomplished without modifying the sections objected to by both the Academy and the AMA. It has been held up in committee by discussion not of the principles of the bill but of administrative methods. He feels that it will pass the House as is when it is reported out of committee. Efforts to prevent passage are still going on.

These subjects were discussed by the 2 committees and the proposed American Legion Child Health program on a community level was also discussed.

Dr. Martin pointed out that our committees were not action committees but were meant to keep each other advised as to programs, policies, etc., and make recommendations to the proper action groups. Academy committees, while notifying the Liaison Committee of their plans, should contact the appropriate Council of the AMA to secure direct action cooperation.

In discussing the American Legion program, it was felt that such a program had definite possibilities if properly directed and if a huge program were not attempted at the start. The original Legion plan was to start in a few small areas which gave promise of successful operation and spread from there. Under such circumstances success is more probable. All medical and allied organizations can and should cooperate to make such efforts a working success.

There was some discussion of legislation pending and it was felt that the 2 groups had similar policies and feelings on all the legislation so far brought up in Congress.

Dr. Martin asked that we use our influence to assure all pediatricians that they were not divorced from the AMA nor at war with that group. In some areas the pediatricians were the most recalcitrant about paying the AMA assessment. Apparently they felt there was no union of interest. Our committee assured him that our organization desired close cooperation of the pediatricians with the AMA and its various component societies.

Respectfully submitted,

PHILIP S. BARBA, *Chairman*

The report of the Résumé of Vote of the Reorganization Report was accepted and approved.

It was moved that the President be empowered to write a letter expressing the views of the Board, in response to the letter sent to them from the pediatric educators.

The Executive Board went into executive session and the following action was taken: That the Central Office be in Chicago or its environs and that it be moved to Chicago itself as soon as feasible.

The Report of the Liaison Officer of the American Public Health Association and National Conference for Cooperation in Health Education was accepted as follows: I have made a suggestion to Dr. Thomas E. Shaffer, as Chairman of the Committee on School Health, relative to relations with the American Public Health Association, because any planning should be with his committee.

I should like to call attention to the resolution unanimously adopted by the A.P.H.A. at their annual meeting Oct. 26, 1949, which is based on the findings of the Study of Child Health Service in the American Academy of Pediatrics. (See the *American Journal of Public Health,* February 1950, p. 228.)

Concerning the National Conference for Cooperation in Health Education, they are in a rather precarious position because the member agencies have given so little financial support that they have not been able to get other support. There is, however, a strong conviction among those who are familiar with the work of the conference that it serves a very useful purpose in providing opportu-

nities for member agencies to keep informed on each others' work and sponsor cooperative action whenever this has been possible. The AMA, for example, has backed up Dr. W. W. Bauer's suggestion that the member agencies contribute $100 annually to give the Conference a sound basis for operation. The question now is whether a reasonable proportion of member agencies "are willing to buy chips as well as to sit in the game." Another possibility has been proposed that the National Health Council furnish secretarial and such assistance as is necessary for effective work of Committees.

With the reorganization of the Academy, it seems appropriate to recommend that an Academy representative should continue "to sit in the game" and the Academy should "buy the chips" for that representative. The significance of such reports as "Suggested School Health Policies" and "The School Administrator, Physician, and Nurse in the School Health Program" is evidence of the value of cooperative action in providing guidance in the improvement of school health. It seems likely that this coming year will be the time when the Conference will either be recognized as fulfilling an essential function or disband.

Respectfully submitted,

HAROLD H. MITCHELL,
Liaison Officer

The Executive Board voted to defer any action on the contribution, suggested in the preceding report, until a later meeting; to retain it on the agenda for the fall meeting.

The Report of the Liaison Officer with the Children's Bureau was accepted as follows: I attended a meeting of the Advisory Committee to the Children's Bureau, held in Washington, January 30 to 31. At the request of Dr. Gordon, who is Chairman of the General Advisory Committee, and Dr. Hubbard, I am preparing a brief report for submission to PEDIATRICS concerning this meeting. Most of the matters considered, however, were routine and not particularly significant to the Academy at the present time, except for a comparatively brief discussion concerning federal aid to medical education in the course of which I attempted to state the present position of the Academy, in accordance with its action at the Atlantic City meeting.

In conversations with Drs. Baumgartner and Daily, I secured indications of an apparently sincere desire to discover points of friction between Children's Bureau and the Academy, also the practicing physicians in the various states, and evidences of willingness to foster better relationship.

A motion was passed at the committee meeting that the attention of the National Committee for the White House Conference be directed to the potential usefulness of the Academy Study of Child Health Services. It was recommended that the White House Conference consider calling a joint meeting with representatives of the Academy of Pediatrics, the Council of Medical Services of the AMA, the Children's Bureau, the Child Health Committee of the A.P.H.A., and the U.S.P.H.S. to discuss this matter.

Respectfully submitted,

CLARENCE H. WEBB,
Liaison Officer

The Report of the Editorial Board was given verbally by Dr. Hugh McCulloch, Editor-in-Chief, and accepted.

The Executive Board voted to authorize the Editor-in-Chief of PEDIATRICS to meet with the Executive Committee of the Section on Pediatrics of the AMA in an effort to bring about an arrangement for use of the Abraham Jacobi Fund.

The question of whether firms who advertise in PEDIATRICS or who have their products displayed at our meetings can put a stamp of approval on their products, "approved by the American Academy of Pediatrics," or a seal other than just the words used in the magazine, was discussed. It had previously been decided to leave approval of such products entirely up to the AMA Committee.

The Report of the Committee for the Improvement of Child Health—Report to the Executive Board for Period Covering Nov. 12, 1949, to March 29, 1950, was read by Dr. Glidden L. Brooks, as follows: Since the last report to the Executive Board, the operations of the Committee for the Improvement of Child Health and its staff have been characterized chiefly by a series of important and drastic changes, all of which have influenced the trend of events and some of which proved to be serious handicaps. Most significant, of course, has been the resignation of Dr. John P.

Hubbard as Director of the Committee. Since much of the work of the Committee has been built around Dr. Hubbard's personal leadership, this has meant a rather drastic revision of plans and activities.

The appointment of Dr. Warren R. Sisson as Chairman of the Committee has provided a fortunate continuity, which runs not only through the Study of Child Health Services but also an eventful year of general Academy activity. Uncertainty as to the extent and exact nature of Academy reorganization, including the selection of an Executive Secretary and Committee personnel, has made general planning on the part of the Committee difficult and definitive planning impossible.

* * *

A meeting of the Committee for the Improvement of Child Health was held in Chicago on January 14 and 15, at which time the program of the Committee was discussed in the light of the circumstances just described. Subsequent events have made much of the detailed considerations of this meeting, including such matters as budget, staff and so forth, meaningless. However, the following activities have been carried on by the staff, which has included Dr. Hubbard until March 1, Dr. Brooks until the present, and Mrs. Lammie until February 15.

I. The Interpretive Report

At the January meeting of the Committee for the Improvement of Child Health, it was voted to ask Dr. Hubbard to complete in final form the first unit of the interpretive report, covering the chapters on Distribution of Medical Care, Private Practice, Undergraduate and Graduate Training in Pediatrics and Regional Planning for Pediatric Education. The second portion of the interpretive report, dealing with State and Community Planning, Cost of Pediatric Service, and so forth, is incomplete and should be enlarged, revised, and published as a second volume. Dr. Hubbard's first volume of the interpretive report has been revised since the committee meeting and is now ready for final editing and publication.

II. Preparation of a "Platform" for the Academy

The Committee discussed at length the need for a statement of a program and guide to action for the Academy, based on the study but shorter and more definitive than the interpretive report. This would be similar in principle to the much publicized 12-point program of the AMA. This is proving to be a more difficult task than it originally appeared. A general statement is apt to be simply a series of harmless platitudes, enlarging and repeating what is already well stated in the constitution of the Academy. Therefore, it is necessary to draft such a platform in terms of definite objectives, together with the manner in which the Academy may be expected to accomplish them.

It is obvious that until reorganization is more complete than at present it is difficult to know what sort of machinery the Academy contemplates for carrying out such a program.

III. State Reports

To date, 29 out of 50 states and territories have published their study reports. In addition, the Western New York region has put out a separate report based on the study findings in that area. These reports are, of course, not a function of the ICH Committee, but the Committee has charged itself with the responsibility for continuing to stimulate those states which have not already done so to publish their reports. In addition, an analysis of recommendations contained in the individual state reports is being prepared for possible use in developing future Academy programs.

IV. The Decentralization Program

The demonstration program in District III continues to be a matter of interest to the ICH Committee. Until the Academy is reorganized and has formally adopted a program for the improvement of child health, it is doubtful that outside financial support can be obtained for this program. The Committee is hopeful, however, that gains already made in the project can be continued until the time is ripe for further augmentation.

V. Roster of Pediatric Residencies

The Committee has continued to maintain a list of approved residencies in pediatrics, together with available openings. Questionnaires as to openings have been circulated twice a year in January and July. The last such questionnaire was sent out in February and to date 162 out of 211 hospitals have supplied the necessary information. It is noteworthy that a year ago we were receiving re-

quests from residents seeking opportunities for training, whereas now we are receiving more requests from hospitals with approved residencies seeking men to fill vacancies. The Committee believes that this activity could be expanded into more than a simple clearing house for information. It is in many respects the first contact a resident has with the organization which in future will represent him in his specialty.

VI. Pediatric Education

The series of meetings on pediatric education, which were started in Detroit prior to the last meeting of the Executive Board, have been continued. Thus far, meetings have been held in San Francisco, New York, Philadelphia, Winston-Salem, Chicago, Kansas City, as well as Detroit. The final meeting is scheduled for the Southwestern area, to be held at New Orleans on April 7. These meetings have without exception been well attended and enthusiastically received, especially by the heads of pediatric departments. Throughout all of them there was evident a strong desire that the Academy continue actively to implement its interest in this field, especially since no other organization exists at the moment capable of doing this as well. One of the important remaining tasks of the staff of the Committee for the Improvement of Child Health is to write a formal report of these meetings, together with recommendations for future Academy activities.

* * *

Present Status

The resignation of Dr. Brooks as Associate Director of the Committee, effective June 1, 1950, is submitted at this time. This leaves the Committee with no staff for the future and makes the submission of a budget of doubtful value until definite plans can be made by the Executive Board.

The funds remaining at the disposal of the Committee from March 1 until July 1, 1950, total $8,788.25. A total of $15,000 has been pledged and is due after July 1, 1950 (NFIP—$10,000, New York Fund for Children—$2,000, Charles H. Hood Dairy Foundation—$3,000). It is questionable how much of this support can be expected in view of the dissolution of the Committee's active staff. Provision must be made for consultation with these foundations in regard to this matter.

The Executive Board moved, seconded and carried that the $1,000 received from Connecticut be made available for the publication of the Interpretive Report, if necessary. It was voted that Dr. Beaven review this document and delete or pass on it from the Board's standpoint. It was moved, seconded and carried that the publication of the Report be delegated to Dr. Grulee, Dr. McCulloch and Dr. Sisson to decide the way of publishing, which gives them full authority to do offset printing or supplement or have a separate publication, considering the distribution.

The motion to reaffirm Article II, Section 1 (a) of the Constitution—"To establish and maintain the highest possible standards for pediatric education in medical schools and hospitals, pediatric practice and research"—and maintain an active part in developing it, was seconded and carried by the Executive Board.

The motion to authorize Dr. Brooks to sell the 1946 Nash was seconded and carried. It was moved, seconded and carried to terminate the lease of the ICH Committee office space, Dr. Grulee to sign the letter. It was decided that Drs. Grulee and Brooks be empowered to consult Dr. Van Riper in regard to funds to carry on the work of the ICH Committee. The functions of the ICH Committee will be carried on by Dr. Sisson in his office and he is to be paid $500 per month for this, plus $1500 per meeting, for a meeting of the Committee.

It was voted to send a letter to Dr. Hubbard from the Board, expressing sincere appreciation for the services he has rendered to the Academy through his efforts in the work of the Child Care Study and the ICH Committee. Drs. Beaven and Bost are to work out something to present to the next meeting of the Executive Board regarding public acknowledgement.

Dr. Henry F. Helmholz presented the following report regarding the need of a study of undergraduate and graduate medical education: I am very happy to be here with you and to tell you how much the White House Committee has appreciated the Study of the Academy. Our fact-finding committee has used it as its source for the Physical Care of Children and the state committees have used the 26 reports that are at present issued.

I think since that last report 2 more have come out, and I have taken it upon myself to write to all the other states, saying how useful these have been to the state committees, hoping that they would hurry with regard to the publication of others.

As far as the Physical Health of the Children, the study has been very useful. It has, however, been rather weak with regard to growth and development and the preventive psychiatric aspects of child care. I think that in speaking with Dr. Mitchell it was extremely difficult at the time to obtain this information. Since that time, through the Mental Health Unit of Public Health Service, 42 of the medical schools have received aid through the Public Health Service for the development of their psychiatric work. So since 1947 there has been a very great increase in this work.

Now in view of the fact that the White House Conference has as its theme the Development in Children of Those Mental, Emotional and Spiritual Qualities That Make for Happy Childhood and for Responsible Citizenship, you see it fits exactly with that part of the Academy study which is weakest, and it seemed to me that here was an opportunity for the Academy to piece out that part of the study that is weakest as its contribution to the White House Conference.

We have had contact with the Mental Health Unit of the Public Health Service, and they are very anxious to know what is being done with regard to the growth and development of the emotional side of the child, and they are willing to help out in this project. The same person who did most of the work in gathering together and bringing together this statistical material is available for this work.

It seemed to me that in view of the fact that this was so much a matter of mental health, that the logical place for the Academy to assist in this would be through its Mental Health Committee, of which Dr. Milton Senn, as you know, is Chairman.

We discussed this matter with Dr. Senn, not from the Academy point of view but from the point of view of the fact that he was in Washington as a member of the Advisory Committee there, and in talking it over with him it seemed logical that if the Academy were willing to help with this study it would be the natural thing to have the association with the Mental Health Committee rather than with the ICH Committee, and that is what we would think would be the logical place for the Academy cooperation.

Dr. Senn is extremely enthusiastic about this. He feels that it would be a very worth while project, and he has said that he would be glad to head up this study.

As I say, when that was brought up, it was not his doing from the side of the Academy, but it was my thought that, in view of the fact that the Academy had done this study, the Academy ought to be represented in this study, that it was something that belonged to the Academy, that we should have the credit that has gone with the development of the other study, which I think certainly is being recognized everywhere as an outstanding contribution to American medicine.

How this can best be done is difficult to say. I don't know what funds are left over from the ICH Committee. I have talked with one of the other foundations that are interested in pediatic education, and the director seemed to think that there might be some money available there, but I am here particularly because I feel that this is something that belongs to the Academy and I should hate to have somebody else do it and the Academy not be in on it.

So I have just left this here. We have worked out a little questionnaire, just to give you an idea of how this thing is to be done, that I will leave with you, and if you have any questions I will be glad to answer them.

This thing really was worked out other than from the Academy, and I do feel that in view of the fact that the Academy has done the health study, it should have part in this study, because I think that the credit for the whole thing belongs to the Academy, and I would hate to see the Academy not have its share in it.

It was moved, seconded and carried that this matter be referred to Dr. Senn, Chairman of our Mental Health Committee, for their study and recommendations which are to be sent to Dr. Grulee as quickly as possible for transition to the Executive Board, by mail.

A letter received from Dr. Katherine Bain regarding an Academy Study to be done in Puerto Rico was read.

The Executive Board moved to sanction the conduct of a study.

A letter from Dr. Alvah L. Newcomb was read concerning associate membership in the Academy for eye specialists who can restrict their work to 90% or more of eye diseases of children.

The Executive Board moved the Secretary be instructed to write Dr. Newcomb to the effect that we are considering such arrangements.

A letter was read from Dr. Ernest E. Arnheim concerning Blue Cross and Blue Shield insurance plans for infants under the age of 3 months.

Dr. Grulee was advised to communicate with Dr. Arnheim to the effect that it is a local problem. It was suggested that the State Chairmen be appraised of this through the District Chairmen.

A letter from Dr. Thomas D. Dublin, Executive Director of the National Health Council, was read concerning the Academy joining with the 30 other leading national health bodies that now hold membership in the Council and thereby furthering the aims of the Council and all of its member agencies.

It was moved that action on this be deferred until the October meeting and the Secretary requested to get further information.

It was moved that the Executive Board favor holding a meeting in Washington, D.C., in the near future and that Dr. Davis supply the Secretary with data concerning the availability of space.

It was moved that arrangements be made to hold the Annual Meeting in Chicago in 1952.

A letter was read from Dr. James C. Carter concerning the registration fee for persons not members of the Academy at the annual meetings.

It was voted that Dr. Grulee should write Dr. Carter, "At the present time, in this process, this principle is in the formative stage and it would be better to try it out for a year or two before we have to increase the amount."

The Executive Board discussed the "Suggested Outline for Academy Organization" as presented by Dr. Beaven insofar as Committees and Representatives are concerned. No action was taken.

The following actions were taken by the Executive Board in Executive Session on Thursday morning:

Revision of By-Laws

Dr. Joseph Wall was requested to make suggested changes in the By-Laws and submit his recommendations to the Executive Board.

Function of the Advisory Committee on Child Health

To act only at the request of the Executive Board or President.

To integrate findings and recommendations of special and/or standing committees at the request of the Board or President.

The Board is agreed that the committee is to have no function or power, to act solely as a deliberative or advisory group.

These are for the instruction of Dr. Wall in preparing the By-Laws to be used for the instruction of the Advisory Committee.

At a later Executive Session the following took place:

Dr. Wall: The Legislative Committee submits no formal report.

It was voted that the Secretary-Treasurer be empowered to appoint a business manager, duties to start July 1, 1950.

Round Table Discussion

THE NEWBORN

WALTER B. SEELYE, M.D., Seattle, *Chairman;* SHEROD M. BILLINGTON, M.D., Seattle, *Assistant*
ELMER LEE TIMMONS, M.D., Colorado Springs, and OTTO GROB, M.D., Detroit, *Secretaries*

INTRODUCTION

Chairman Seelye: No subject lies closer to the heart of the pediatrician than that of the newborn infant. Pediatrics has always been deeply concerned with the management of the infant during that trying period immediately following birth, when certain anatomic and physiologic adjustments must be quickly and smoothly made if the child is to survive. Here indeed is the supreme challenge to the physician who must promptly and efficiently recognize, correct and treat the defects, deficiencies and diseases which may handicap the infant.

Certain aspects of the newborn infant are of such magnitude that they lend themselves to separate panels and round tables. Among these are: the premature infant, hemolytic disease of the newborn, anemias of the newborn, epidemic diarrhea of the newborn—all of which have been presented at recent meetings of the Academy. These will be omitted from our discussion today, which will be directed toward consideration of the following topics:

1. Accidents and Trauma Incident to Birth
2. Infections
3. Feeding. The Psychologic Aspects of Mother-Infant Relationships

1. ACCIDENTS AND TRAUMA INCIDENT TO BIRTH

Much has been recently added to our knowledge of the effects of interference with the supply of oxygen to the tissues of the fetus before and during birth, and to the infant after delivery. Clifford has clearly shown that injury resulting from anoxia is widespread, involving physiologic and pathologic changes throughout the entire body. These have been summarized as "congestion, edema, hemorrhage and death of tissue."

Intrauterine anoxia is presumably due principally to pathologic conditions of the placenta which result in the majority of instances, in premature separation of this organ. Approximately four fifths of the total number of cases of intrauterine asphyxia are said to occur as the result of premature separation of the placenta.

Anoxia in the fetus during passage through the birth canal may result from any of a number of causes of interference with the supply of oxygen to the placenta and/or interruption of the circulation within the placenta or in the umbilical cord. Prompt recognition and correction when possible of such interference are matters of extreme urgency to the physician; he must deliver the infant as quickly as is consistent with good obstetric procedure when it has become apparent that oxygen is no longer reaching the fetus in sufficient amounts.

Failure to establish promptly an efficient ventilation of the lungs with adequate exchange of oxygen and carbon dioxide results in prolonging and exaggerating the normal physiologic state in which the fetus has existed up to the time of birth. While the need for oxygen during fetal life may be quite low, the infant at birth must establish, and in a relatively short time, adequate oxygenation of his tissues if he is to survive. Anoxia in the immediate postnatal period may result from injury which has occurred or has been initiated before or during birth, or from inability on the part of the infant's previously inactive respiratory system to take up its normal functions. A better understanding of the cause and effect relationship of maternal analgesia and anesthesia to narcosis and anesthesia of the infant has made possible the encouraging reduction of incidence of asphyxia from these causes. During the past year there have been no infant deaths attributable to maternal analgesia or anesthesia at King County Hospital. The Department of Obstetrics at the University of Washing-

From the Annual Meeting of the American Academy of Pediatrics, San Francisco, Nov. 14 and 15, 1950.

ton School of Medicine has established the following procedure,* based on the premise that "less analgesia—more regional anesthesia" will result in fewer instances of narcosis of the infant:

1. Nembutal 100 mg. is given orally when—and not before—labor is well underway, i.e., the cervix is dilated at least 3 cm. This may not be repeated more than once.

2. Demerol 100 mg. and scopolamine 0.4 mg. are given by subcutaneous injection when labor has progressed satisfactorily.

3. Metacaine 15 mg. is given by low spinal injection at the beginning of the second stage of labor.

A study of the correlation of this type of management with the time the infant takes his first breath (first inspiration) and when he first cries is being undertaken. As soon as the head is born a stop-watch is started and these time intervals accurately determined. These intervals are being tabulated against the amounts of analgesic and anesthetic agents used. This is of course repeating the work of Eastman, Cole and others. We hope it will shed further light on the question of the influence of maternal analgesia and anesthesia on the newborn infant.

Saddle block anesthesia is not without its dangers however. Due cognizance must be taken of the effect of low spinal anesthesia on the maternal blood pressure. Andros and his group at the Chicago Lying-in Hospital have reported a fall of the systolic pressure to levels of 80 mm. Hg or below in 13.7% of women who were delivered under this type of anesthetic. Similar depressions of blood pressure were found by Hingson and his associates at the Lying-in Hospital of Philadelphia. They report an incidence of 10% in a somewhat larger series and present evidence that fetal anoxia resulted when the maternal systolic pressure remained below 80 mm. Hg for 5 minutes or longer, hinting that under these circumstances the tone of the uterus itself is greater than the arterial blood pressure. Eastman and others, however, feel that the advantages to the infant outweigh the hazards of this lowering of the blood pressure.

Other causes of failure on the part of the infant to initiate respirations may be mentioned. A respiratory center which has been damaged by anoxia either before or during delivery cannot respond to the normal stimulus provided by an increasing H-ion content of the blood. Obstructed airways from aspiration of greater than normal amounts of amniotic fluid, or of blood or mucus prevent access of air or, during efforts at resuscitation, other oxygen-containing gases, to the lungs. Though there is some disagreement as to the exact manner in which it is best done, i.e., by bulb-syringe suction, by intratracheal aspiration, by direct visualization by means of laryngoscopy, by bronchoscopy, by milking the trachea or by gravity (postural drainage) alone and so on, everyone agrees as to the urgent necessity of establishing a free airway in all newly born infants, whether or not they show signs of asphyxia. Our own preference is for the method that accomplishes its purpose with the least delay, since it must be done before the first breath is taken, and the least trauma to the infant, this method consisting in most cases of removing by gentle suction any excess fluid contents of the oro-pharynx and placing the infant in a head-low position to favor drainage by gravity of any subsequent accumulation. Further discussion of this subject during the question and answer period is anticipated.

Anoxia during the extrauterine period may be the result of congenital anomalies and malformations of the upper respiratory tract, particularly of the larynx and upper trachea (laryngeal stenosis, tracheo-esophageal fistula and the like). It may be due to malformations of the lungs or the circulatory system. Herniation of abdominal viscera through a defect in the diaphragm may interfere with expansion of the lungs sufficiently to preclude adequate aeration of the pulmonary blood. Anoxia may also result from damage to the central nervous system following intracranial hemorrhage.

That the asphyxiated infant who survives the neonatal period without manifest neurologic sequelae may not have come through the birth process entirely unscathed has been called to our attention again by Stevenson. We are reminded that central nervous system damage may not be clinically apparent for several months and that "it is dangerous to assume that a newborn baby is unharmed because he appears well when he leaves the hospital." This has particular significance in those instances when we are asked to put the stamp of approval on babies who are to be adopted.

Discussion

Dr. E. R. Murphy, Salt Lake City: Just how complete control do you have over your obstetricians?

Chairman Seelye: We have as near an ideal liaison between the 2 departments as I think can be

* Russell R. de Alvarez, M.D., personal communication.

established. We are a new school and are starting off idealistically. We have what many have been striving for years to attain: better coordination between the 2 departments. Weekly rounds are made together in the newborn nursery, the Chief of the Obstetrics Department and his resident, with the Chief of the Pediatrics Department and his resident. Our residents in pediatrics rotate on the newborn service and are on call for section deliveries, premature deliveries, deliveries of diabetic mothers and so on.

Dr. O. Grob, Detroit: About the aspiration of nasopharyngeal secretions: what method do you use?

Chairman Seelye: We prefer to use a soft tipped rubber bulb syringe in the mouth, and a small catheter in the pharynx.

Dr. R. E. Nutting, Duluth: Do you let the nurses do this?

Chairman Seelye: Yes, the nurses are trained very carefully. I think many of us have seen newborn infants with traumatized pharyngeal and oral mucous membranes from too hasty and crude sucking-out methods.

Dr. E. H. Christopherson, San Diego, Calif.: We have had trouble with a rather large percentage of our cesarean babies. About a third of them have been getting into some sort of respiratory difficulty. The interesting thing is that many of them are brought to the nursery in very good condition from the operating room but within a period of a few hours or even the next day dyspnea develops and you can definitely demonstrate anoxia. It is some sort of irritation that causes trouble later, and not immediately, from the aspiration of amniotic fluid. We have started aspirating the stomachs of cesarean babies. I would like to add that those babies received oxygen from birth.

Dr. Billington: In Seattle, Dr. Palmer at the Virginia Mason Hospital has charge of a large number of diabetic mothers. Up to the present time I have cared for about 18 babies delivered of those mothers by section and have not seen this excess accumulation of fluid. We have not seen evidence of aspiration of gastric fluid. Furthermore we haven't had any babies with hypoglycemia. Except for the fact that those babies felt definitely different—they all have a soft, pudgy feel—they do not seem different from other babies. They have been a little smaller and possibly have had a more difficult time but no more than you would expect from their size and the fact that they were delivered a little early. Furthermore in a few cases we have tried giving steroids in the last portion of pregnancy and during delivery. We haven't felt that in the few we have tried it on it has made any difference.

Chairman Seelye: Actually much of this delivery room technic is only of theoretic interest to us because we as pediatricians are not present during the first few minutes of the baby's life. But I feel that a better understanding of the difficulties sometimes encountered will result from our reviewing these topics from time to time. What is the opinion of the group in regard to how we may better our understanding in our relationships with the general practitioners who are delivering 50% or more of the babies?

Dr. E. R. Murphy, Salt Lake City: That seems to be an impossible thing to solve in an overstaffed hospital.

Dr. Billington: I think the antagonism between the obstetrician and the pediatrician is a very real thing in every community. Certainly in private practice in Seattle we do not have the ideal situation that Dr. Seelye has outlined for the University group. I think it is a slow process of taking opportunities to present statistics to them and convincing them that there are safer ways of delivering babies and attempting to create local interest in ways that are less hazardous. I think as young men come into each community they will in time help to elevate the standards.

Dr. Edith N. Meyers, Oakland: We have always considered the problem of the apparently well, full term baby who has severe respiratory distress as atelectatic, but recently pathologists are telling us, from autopsies, they are finding many of these babies with undeveloped air sacs in their lungs. I would like to hear some discussion of this.

Chairman Seelye: There seems to be some disagreement as to the actual pathology involved. I think we are agreed that atelectasis is secondary in most instances. It is a difficult thing to prove, in view of the difference of opinion among pathologists, that there is actually a failure on the part of development in even small premature infants as long as they apparently are ready to expand their lungs and to take up the exchange of gases.

Dr. E. T. McEnery, Chicago: I would like to say a few words about the obstetrician and pediatrician cooperating more in the dispensing of training to men interested in the care of the newborn infant. A recent book by Stone, on the care of the newborn infant, states that the obstetrician should look after the infant during this period, as the average pediatrician does not have the opportunity

Aerobacter aerogene 4%
Salmonella 4%
Proteus 4%

In a review of the literature they were able to find 35 cases which met their criteria for primary septicemia. The etiologic agents by percentage were: streptococci, 50%; colon bacillus, 27%; staphylococcus, 18%. The other cases were caused by Salmonella and mixed infections. They conclude that the obscurely ill newborn infant must be suspected of septicemia. Blood cultures should be taken, and then therapy should be started. With the knowledge they have given us we should employ "blanket therapy." In this connection, Dr. Perin Long has recently made recommendation for therapy of choice in dealing with specific organisms. It therefore seems best that this "blanket therapy" include: penicillin G (vs. streptococcus and staphylococcus); chloromycetin (vs. proteus vulgaris); and aureomycin (vs. colon bacillus, staphylococcus and aerobacter aerogenes). We suggest referral to Dr. Long's article for dosages and schedules: J.A.M.A. **141**:5, 1949.

2. Infections acquired by person-to-person transmission of pathogens: by droplet.

Efforts at reducing the incidence of this type of infection must be directed along 2 channels: reducing the number of people who contact the baby and elimination of individuals with clinical signs of respiratory infection. The use of rooming-in technic goes far toward accomplishing the first of these. The careful supervision of the nursery personnel is essential to an attempt to accomplish the elimination of those with respiratory infections. Their actual elimination brings up an economic problem whose practical solution seems to lie in utilization of less expensive part-time help, namely, nurses' aides.

3. Infections acquired from pathogens present in the air.

This source of infection, as Dr. Clifford has stated, is recognized but difficult to evaluate. The American Academy of Pediatrics' Committee on Fetus and Newborn has made definite recommendations on attempts to disinfect air. Dust should be controlled by oiling of floors, bed clothes and other textiles. Complete air-conditioning is desirable in newborn nurseries. The relative merits of ultra-violet irradiation and glycol vapors have yet to be established. Installation of either of these must be done under competent engineering supervision.

4. Infections acquired from physical contact with infected personnel or material.

Again rooming-in technics, simulating conditions of home delivery and neonatal care, seem to meet many of the prophylactic needs in the category. Rooming-in technic is far from universal acceptance and will meet with practical objections stemming from limitation of physical facilities and from psychologic considerations of mothers and hospital personnel. We therefore must direct our attention toward providing as much individual isolation for the baby as is practical in present physical setups. Nursery personnel must be propagandized with regard to attitudes and practices toward this end.

5. Infection acquired from the ingestion of pathogens contained in the food.

The recommendation of the Committee on Fetus and Newborn for the terminal sterilization of formula in the individual feeding bottle with cap and nipple assembled has been a major factor toward eliminating this source of infection. Pediatricians in each community should make a concerted effort to reduce the variety of formulae prepared, and as a body, they must assume responsibility and interest in the proper execution locally, of these recommendations.

Discussion

Dr. Edith M. Meyers, New Orleans: We have attempted in our hospital to work with the personnel to the end that we may eliminate masks in accordance with the standards of the recommendations of the American Academy. We have run into the difficulty of trying to find enough women, nurses and nurses' aides with negative throat cultures to staff our hospital. I wonder what the experience of other hospitals is in this regard?

Dr. E. T. McEnery, Chicago: We do not use masks in our nurseries and I do not feel the incidence of infection has increased. Ten years ago the late Dr. Blatt did some very extensive work on

the proper type of mask to wear. The type of mask that he devised was perfect. The mask was very fine but the nurses' technic was poor and the mask did not work so well. The nurse, on removing the mask, would place it in her pocket, leave the nursery and when she returned would take it out of her pocket and put it on. This was poor technic and the more she handled the mask the more she contaminated everything she touched. If nurses can be trained to keep their hands from their faces, the protection is greater.

3. Feeding

Chairman Seelye: Although pediatricians are agreed that more breast feeding would be a good thing, no one does much about it. I hasten to add that this is not literally true lest I bring down the wrath of those few who diligently strive to promote this natural method of infant feeding. Complete confidence of the new mothers must be won if the incidence of successful breast nursing is to be increased. Something new has been added in the Rooming-In Plan which is being tried in many parts of the country. The apparent trend toward an increased number of successfully breast-fed babies which has resulted when mother and newborn are allowed to share a room gives promise that perhaps at long last we are on the right track. When this and other methods fail, however, we still must have recourse to artificial feeding. Having passed through the stages of percentage and calorie feeding to the relatively simple formula writing of today, further progress in infant feeding is indicated in the current adoption of the so-called demand schedule. I am going to call on Dr. Billington again to review for us the newer thoughts in this important phase of our responsibility to the newborn infant.

Breast Feeding

Dr. Billington: At the present time, we have no factual information as to the over-all trend in breast feeding. Most of us do have the impression that as time goes on fewer mothers are breast feeding. Dr. Katherine Bain reported in 1948 on the nation-wide survey of breast feeding in hospitals which was a part of the American Academy of Pediatrics' Study of Child Health Services. The percentage of hospitals reporting was sufficiently high to make the statistics significant. Data on 39,000 babies at the time of their discharge from the newborn nursery revealed that 38% were totally breast fed, 27% were partly breast fed, 35% totally bottle fed. Her break-down of these figures revealed a smaller percentage of breast feeding in or near metropolitan areas. I believe it fair to state that a large majority of the 27% who go home on breast and bottle are entirely bottle fed by 6 weeks of age. In Seattle we note a marked difference in the number of breast-fed babies in the County Hospital group of patients and in our private patients. Twice as many mothers in the County Hospital group nurse their babies.

Attempts to increase the incidence of breast feeding must begin in general community education. We should use public relations methods to have movies, newspapers and speakers utilize every opportunity to sell the idea that breast feeding is a natural, safe, desirable method of nourishing the baby.

The next step falls upon the combined shoulders of the obstetrician and the pediatrician in providing mental and physical preparation in the pregnant woman. Pediatricians must seek and exploit opportunities to talk before groups of obstetricians in efforts to stimulate their interest and cooperation. The individual expectant mother should be convinced that nursing her baby is an integral part of biologic fruition. She has had motherhood as her goal since the dawn of her femaleness. We must instill in her the idea that nursing her baby will really make her feel and be biologically complete. In the last months of pregnancy routines of nipple massage and care may offer little toward avoiding cracked nipples but certainly provides good psychologic benefits. Retracted nipples often can be corrected by the use of a plastic or glass breast shield, with a central aperture for the nipple; this is worn over the breast and under the brassiere in the last months of pregnancy.

The next phase in a program aimed at increasing breast feeding lies in the orbit of hospital personnel: pediatrician, obstetrician and nurses. Basic principles of lactation must be considered in all arrangements which are made. The primary principle of lactation is that emptying the breast is stimulating. Hence the baby must be awake and hungry when carried to breast and the baby's failure to empty the breasts must be corrected by manual or mechanical emptying. Engorgement on the third or fourth postpartum day may make nursing difficult for the infant and may depress lactation by retention of milk within the breast. Harold Wahler of the British Hospital for Mothers and Babies, London, has reported recently on the use of small doses of synthetic estrogens on the second and

third day to check this sudden outburst of lactation. Frequent stimulation of lactation is desirable, yet many hospitals substitute a 2 or 3 A.M. bottle for the nursing at breast. This practice not only reduces the number of breast emptyings in 24 hours, but often so fills the baby that less interest is taken in the next breast feeding. The erratic feeding habits of newly born infants are generally recognized but few hospitals have adjusted feeding routines for newborn infants in the light of this knowledge. More will be said of this later. The factors and attitudes we have mentioned, and others which may contribute to increasing success in breast feeding, must be drummed into the consciousness of all hospital personnel who contact mothers and newly born infants and must be the basis of practical hospital arrangements.

No discussion of breast feeding in these days can be complete without mentioning the important role that all hospital personnel play in bolstering a nursing mother's morale. Often a careless, discouraging remark by a nurse or a doctor abolishes a mother's chances of developing adequate lactation.

Substitution Feeding of the Newborn Infant

In recent years there has been a steady decline in the variety of formulae used as substitutes for breast feeding. Simulation of breast milk has been the aim in the preparation of most formulae. Cow's milk forms the basis of most formulae. Holt, Powers, Levine and Gordon have all stressed the intolerance of premature and immature babies for cow's milk fat and have advocated reducing or substituting this fraction in cow's milk formulae. We must be alert to this cause of indigestion in full term newly born infants.

McCulloch and McMahon strongly advocate the use of evaporated milk without added sugar. They advance several reasons for this. The babies have seemed less liable to diarrheal upsets. They believe babies so fed have better turgor and seem more active. They also suggest advantages in the form of hungrier babies who eat with greater gusto and have augmented conditioned reflexes to the pattern of "hunger, eat, and satisfaction." They admit slower weight gains in the first 3 months and advise forewarning mothers. In further support of McCulloch and McMahon, Gerstley in 1945 reported on the rachitogenic possibilities of too rapid growth and weight gain in the first 6 months.

Much of our role as pediatricians in helping a mother with her infant in the first year consists in education about foods and in the creation of attitudes. I feel a mother profits by knowing what comprises the total diet for her infant. The constituents must still be present in her older child's diet, in one way or another. Therefore I suggest we reserve total formulae for their original purpose—the mother who cannot profit by education and whose baby might suffer malnutrition.

For obvious reasons we should reassure the mother who must resort to a substitution feeding for her baby. We must inform her of the nutritional adequacy of substitution formulae. She should be told to hold and handle her baby at feeding time as nearly like breast feeding as she can. Mention should be made of alternating the arm in which she holds the baby at each feeding.

Self-Demand Feeding

The newborn infant has recently left a warm, well cushioned environment in which his food was constantly being supplied. The physical rigors of birth and the subsequent adjustments are tremendous. The seeds of insecurity certainly seem well planted and will be fertilized by any additional trauma or frustration in the newborn period. We are guilty of superficiality if we attempt to impose features of our civilization so early in life. In Western culture, denial and self-sacrifice are extolled as virtues. Actually they are attributes acquired by experience, and serve the more civilized person in getting along in his society. They need not and must not be imposed on the inexperienced and insecure newborn. The viewpoint must be shifted. The baby is born a savage: unfitted for experience in frustration and denial. We must concentrate on creating a stable sense of security in the newborn infant.

The newborn infant has a very limited orbit of experience from which to derive security. The principal component of this experience is hunger, eating and satisfaction. The warm, well-bundled baby has left only hunger with which to be frustrated. The newborn infant experiences hunger at various times. Food must be supplied at these times in order that frustration and consequent insecurity may be avoided. The repetition of this experience should assure us a secure newborn infant.

Few hospitals are coping with this important phase of newborn activity. The arbitrarily fixed schedule results in sleepy babies being offered food and hungry babies being denied satisfaction. We as

pediatricians, interested in achieving this fundamental security for the baby, must await their discharge from the newborn nursery. Rooming-in technic avoids this unfortunate delay.

Early self-demand feeding does not condemn the family to an uncivilized older infant. The process of civilizing the savage infant is certainly more logical and successful if the infant has the poise afforded by basic security. Self-demand feeding results in the rapid emergence of rhythmic hunger and 3- or 4-hour schedules are naturally achieved by a few weeks of age. Thereafter civilizing processes, applied with an art of gradualness, are successful in achieving a cooperative member of society.

Rooming-In

Rooming-in has received ever-growing attention from the profession and the laity. The pendulum is in full swing toward more natural childbirth, more natural feeding and more natural mother-infant relationships. A large experience with rooming-in has been had at Yale, Jefferson, Duke, Georgetown and other hospitals. In Seattle we have had a limited occasional experience with this technic. At nearby Madigan General Hospital at Fort Lewis, a fairly large experience with rooming-in has been had. In the 6 months from April to October of this year, 850 women were delivered. Rooming-in arrangements were provided for the infants of 355 of these. Three hundred thirteen mothers (88%) were totally breast-feeding their babies at the time of discharge. As elsewhere, it was found advisable to mingle primiparas and multiparas. Rooms contained from 2 to 7 mothers, each with her newborn infant.

Institution of this program met with considerable hostility from the nursing personnel. Intensive indoctrination by enthusiastic proponents of rooming-in overcame this initial deterrent. The nursing personnel are now enthusiastic advocates. Furthermore it has been possible to adequately staff 16 patients and their babies, with 2 nurses and a ward maid, for three 8 hour shifts. The ward maid is covered by the night supervisor from the "orthodox" section of the obstetric floor. Babies are placed in bassinettes at the mother's bedside at 12 to 24 hours of age. Thereafter mothers are instructed and supervised in the baby's care for 24 hours. Generally, the mother then assumes the full care of her baby. The mothers are indoctrinated in self-demand routines.

This group of mothers was composed of volunteer members. Most of them were eager participants. With few exceptions they left the hospital pleased with their experience. Acceptance of this method of hospital care of mother and baby is increasing. Local acceptance of this technic necessarily will depend upon community attitudes, physical facilities and realization of its desirability by doctors and nurses.

We feel that rooming-in offers a solution to many problems of the newborn period. It provides a mother with confidence when she goes home. Rooming-in offers the best chance of establishing security in the newborn infant. Many sources of infection at this stage are minimized and some eliminated.

Discussion

Dr. A. D. Wert, Portland: I believe that the primary problem is training the obstetricians or getting the obstetricians and the general practitioners to understand the importance of breast feeding before attempting any general lay education, because some of the men who have the largest obstetric practices seem to be the ones who find it much simpler to tell the mothers, even though the mothers do desire breast feeding, that they will give them stilbestrol, hot packs, and so on to control normal lactation. If we go ahead and start our lay education I think that we are going to have difficulty at that level in getting cooperation from other members of the profession.

Dr. Billington: We are fortunate because there is tremendous interest in rooming-in, in less manipulation of the baby and in letting them feed when they are hungry. The whole trend is receiving wide publicity. It is in lay publications, in talks that are being given to prenatal groups, and in talks that pediatricians are giving before parent-teacher groups. I think if we take advantage of this general interest, this trend, we have an opportunity to create considerable interest in the laity in breast feeding and the obstetrician will have to just tag along.

Dr. Alma M. Sullivan, New Orleans: I see the advantages of rooming-in, but I think we should have the facilities set up before we do all this campaigning.

Dr. Billington: I think the only thing that will create the setup will be the public demand for it. It is places like Yale and Duke that have created the interest, but for the country at large we must create lay interest.

Chairman Seelye: Dr. Norman W. Clein will discuss allergy in the newborn period.

Dr. Norman W. Clein, Seattle: Early diagnosis of allergy may help in the prevention of many major allergic symptoms that develop later in life. If you know an infant is allergic you can lay out a plan that may prevent him from suffering many unnecessary symptoms as he grows older. If one parent is allergic, about 50% of the offspring will have allergy manifestations. If both parents are allergic, all the children will have allergic diseases in one form or another at one time or another. Ratner has demonstrated that by avoiding the highly allergenic foods, inhalants and contacts in the pregnant woman, the degree of hypersensitivity in her infant may be minimized.

Eighty-two per cent of allergic infants develop their first allergic manifestations before they are 4 months old and 89% develop them by the time they are 1 year of age. Symptoms are primarily of three types: (1) rash (eczema), (2) vomiting (pylorospasm) and (3) gastrointestinal distress characterized by persistent colic, gas, diarrhea or constipation; more rarely, asthma, perennial rhinitis, hay fever or hives.

These first allergic symptoms may be caused by foods, contactants or inhalant antigens contained in house dust. Since the infant's diet is limited it is a fairly simple procedure to eliminate, one at a time, the various foods. Milk, the most common allergic factor, should be eliminated first and an animal-free substitute used, such as Mullsoy or Nutramigen. The mistake is usually made of trying various cow's milk formulae first. If the infant is allergic to milk he will not tolerate any type of cow's milk preparation. Orange juice, fish oils and wheat are also frequent allergens. Synthetic multiple vitamin preparations will prevent many of the first allergic insults which are due to orange juice or fish oils.

Chairman Seelye: Thank you, Dr. Clein. Our time is up. I am going to close this Round Table with the following recommendations:

1. Let us try to have fewer babies in individual nurseries. The recommendations of the Committee on Fetus and Newborn are for not more than 12 babies, with 24 square feet per infant, in each nursery.
2. Let us urge our hospitals to provide isolation and suspect-isolation nurseries.
3. Let us try for closer liaison between the obstetrician and the pediatrician.

Pediatrics

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SPECIAL SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

AN OPEN FORUM

PAUL A. HARPER, M.D., *Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

COMMUNICATION FROM DR. WILLIAM G. LENNOX

The following communication is from Dr. William G. Lennox, Associate Professor of Neurology, Harvard University, and Director of the Seizure Unit of the Children's Medical Center.

DEAR DR. HARPER:

I enclose a portion of an address, "Epilepsy Then, Now and A Century Hence," delivered at the Centenary of the Boston University School of Medicine. In the belief that the subject discussed will become increasingly timely, I request space for it in "The Pediatrician and the Public." Pediatricians occupy a strategic position with respect to genetics and childbearing and, because of their associations, pediatricians should be unusually youthful minded and forward looking.

(signed) WILLIAM G. LENNOX, M.D.
Boston

A FRESH FRONTIER FOR MEDICINE

From our little Mount Pisgah we have gazed hopefully toward the Promised Land of Epilepsy Control. Now we must descend to the common plain of economics. Fruitful research in any field depends primarily on inspired minds, but money, with its supporting stable politico-economy, seems increasingly important. What will be the state of the world a century hence? Who or what threatens its stability?

At the moment we fear the power of the fissured atom. We physicians envy atomic scientists with their billions to spend, and we feel superior because our labors do not

engender fears of catastrophic destruction. And yet, what will people think of us a century hence? By then, we are told, the population of the earth, excessive with respect to its natural or man-made resources, will present a wider and more insoluble menace to peace and prosperity than the split atom. For this menace our profession will be chiefly to blame.

Medical science and public health forces have wonderfully reduced the scourge of sickness and death; but the doubled life span means a doubled population—and, for the added portion of that span, economic unproductivity. A passion for prolonging all lives, including the genetically unfit (coupled with war's destruction of the fit), has violated nature's plans for humanity's improvement. Flattered for past achievements in prolonging life, we physicians ignore the complementary problem of excessive births. We see no danger and cry no alarms. Knowing most about human genetics and the physiology, endocrinology and psychology of reproduction, we nevertheless have not grappled seriously with the vast problems involved in widespread efforts towards the limitation and the genetic improvement of the human breed. Hence, we delegate the task of eliminating the surplus to those ugly reapers, war and famine, and thereby resign our bright hopes for a better economy and a healthier world.

I speak with feeling because of my experience in a land where the disease of numbers is not (as with us) in the future, but is already chronic and apparently irreversible. In youth's fresh enthusiasm for saving of life, I went as a medical missionary to China where the opportunity seemed greatest. Realization came only gradually that China already had too many mouths for the available food. (A family is said to consist of so many mouths—not persons.) Even disease rampant could not keep the number in check. More food meant only more mouths. Births did not go down as the standard of living went up. Chinese doctors, relatively prosperous, had more children than their poor patients. In short, China needed not more but fewer (and better) lives. The diseases dangerous to her economy were not those that kill quickly, but those that only cripple. For countries like China and India, crushed by their own human load, the development and widespread use of a cheap, foolproof means of contraception could give the healthier and the better life that neither industrialization, a stable government nor dollar aid by the billion can ever give. Failing such help, congested and desperate misery, spreading like an infectious disease, could in time make a "one world" of misery.

In our country the excess of births over deaths was greater in the last decade than in any that preceded. Yet our immediate problem relates more to the quality than to the quantity of our people. Because families of low intelligence are the largest, geneticist Burt estimates that the intelligence score of the population falls by two points each generation. Conceivably, a welfare state might accelerate the decline. By means of prophylactic inoculations and modern germ-killing medicines, we unmercifully prolong the lives of imbeciles (clock cases without works) whose only relief is death, and thereby bar our institutional doors to many who might be restored to health and productivity.

We have time to meet the creeping paralysis of population if our medical and social scientists, our statesmen and our theologians will wake from their dreaming. The depth of that dreaming is illustrated by this fact: in Massachusetts and Connecticut, a physician is fined and jailed for exercising his God-given conscience and common sense in giving contraceptive advice to his patient. That without this advice the mother may die is no defense. Repeated efforts have failed to break this "religion"-inspired stranglehold.

Atomic control could be secured by joint action of a few hundred men, control of procreation will require the cooperation of the millions.

In one respect, this danger, as yet only dimly realized, may be opportune for our profession. Many medical problems are solved and many diseases are brought under control. Physicians and researchers require fresh outlets for adventurous thinking and acting. This disease of over-population offers a fertile field for those who can see beyond the walls of office and laboratory. The housing shortage is becoming increasingly acute in the exclusive residential district of "Ivory Towers." The man of science must increasingly be a world citizen. Geneticists must look beyond the fruit fly to man, a biologic subject they and our medical schools have conspicuously ignored.

Procreation and its control, and the upgrading of population are world-wide projects of challenging breadth and complexity. Here is a new frontier for medicine allied with economics. Have we the vision and the initiative to lead toward what we all hope will be a happy earth, comfortably covered with persons possessed of good bodies and minds—and good will?

TRENDS

By JOHN P. HUBBARD, M.D., *Contributing Editor*

This and subsequent descriptions of events and trends are intended to be unbiased and factual, presenting both sides of controversial matters so that conclusions may be formed from critical appraisal of things as they are. These statements do not necessarily reflect the opinion of the writer nor are they to be interpreted as official opinion of the Academy.

THE HEALTH COUNCIL—NATIONAL, STATE AND LOCAL

IN MOST of the reports of the Academy's Study published by the individual states, emphasis has been placed upon the development of health councils from the pediatric viewpoint. One of the outstanding features of these state recommendations is the importance given to bringing together at the state and community levels all those agencies which have a primary interest in child health. The following quotation from the Louisiana report is characteristic of many: "Cooperative planning and action, state-wide and in local communities, can help to meet the needs of Louisiana's children. A Child Health Council, created by the State Medical and Pediatric Societies, should include representation from all medical and lay groups interested in child health. Local councils should be fostered by the state groups."*

These objectives do not stand alone, but on the contrary are closely related to a growing trend. Those who are responsible for activating the recommendations of state reports will find support from the increasing interest in health councils throughout the country and will, at the same time, add to the momentum of this significant movement.

In this connection particular attention should be given to the National Health Council, a voluntary association of national health agencies joined together for the purpose of common planning for the improvement of the health services of the country. The Council today is taking an active role in promoting community organization for health. Its immediate objectives as stated in its informational bulletins are the following:

1. The creation of new state and local health councils and cooperation with existing councils to secure more complete and more efficient health services;
2. The promotion of full time health departments with competent professional staff;
3. The recruitment and training of personnel for health council work.

As a step toward these objectives an Inter-Agency Institute on Local and State Health Councils was held under the auspices of the National Health Council, November 29-30, at Princeton, N.J. A pamphlet summarizing the highlights of this meeting has recently been published; it contains much of interest to anyone who is concerned with the development of child health councils.†

A few excerpts from the summarized proceedings of this conference demonstrate the close relationship of the opinions expressed there and the statements coming from many quarters in the Academy:

"A health council is a meeting ground for all forces making for good public health in a community; it is a working together—surveying the whole broad picture of community health needs, discovering unmet needs and developing plans for meeting those needs,

* "What We're Doing for Our Children." The Study of Child Health Services in Louisiana, 1560 Line Avenue, Shreveport 39, La.

† "Quiet—People at Work." Published by the National Health Council, 1790 Broadway, New York City 19.

demonstrating new services through member agencies; it is developing a well-rounded community program and keeping public interest in health at a high pitch. It is easier for a united group to accomplish this than for many isolated agencies all trying individually to bring about the same results."*

Dr. Henry B. Mulholland (Council on Medical Service, American Medical Association) gave two reasons for the interest of the American Medical Association in the formation of health councils—the first, because it felt that problems of medical care and health can very often best be solved at the local level; and second, because the "getting together" of various agencies and various individuals on a local level is important. It is important for two reasons—to find out what the health and medical care needs are and to get something done about them.

Dr. Thomas D. Dublin, Executive Director of the National Health Council, pointed out that not so very long ago the doctor was essentially the sole person in a community who had any special skills in health promotion, diagnosis and treatment, but today this no longer holds true. The doctor now makes up only about 1 in 7 or 1 in 10 of all the professional people who are concerned with health services. In addition, a huge volume of physical and other resources are established in most communities to provide the means necessary for people to solve their health problems.

We have on the one hand a huge volume of skills and resources which are not being effectively utilized and on the other hand a population which wants to do something about its health. And yet we have this tremendous gap between the resources and the utilization of these resources. The job before all of us, professionals and citizens, is to get together and see that resources are used to solve health problems.

Miss Winonah Darrah, describing the development of the Monmouth County (N. J.) Health Council, emphasized, as did many others throughout the meeting, that the organization of a health council depends so often upon individual leadership. She stated that one of the main reasons for the development of the Monmouth County Health Council arose from the vision of a physician, the late Dr. Stanley Nichols, who believed that health was the individual's responsibility and that any program set up, whether it be a guidance program, or a service program, should be representative of the people.

Some practical answers to the question of getting community action were given by Dr. Roscoe P. Kandle, Director of Field Services of the American Public Health Association: Initial studies should be as complete as possible, and might include an evaluation which would have the sources of strength, some of the limitations, the human and natural resources, the variations in culture, the presence of other community problems that indirectly relate to health, and the presence of opposition groups and vested interests.

The council should evolve a plan of attack. It is desirable to select for the first problem one that has some reasonable expectation of success. The initial successes or failures may have a good deal to do with getting anything else done or not. The plan of attack should be as comprehensive as possible and should make intelligent use of all public information media in order to motivate as large a segment of the community as possible.

Councils have a responsibility for continuous evaluation of their assistance to community leaders through a periodic reappraisal of the community needs.

The ultimate success of the council depends on the degree to which the community identifies the council as being the community's own mechanism rather than something thrust upon the community.

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* "Stepping Stones to a Health Council," by Yolande Lyon. Published by the National Health Council, 1790 Broadway, New York City 19.

PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

MYRON E. WEGMAN, M.D., *Contributing Editor*

MIDCENTURY WHITE HOUSE CONFERENCE ON CHILDREN AND YOUTH

THE five White House Conferences represent in no small degree the stages in the development of pediatrics in the United States. The first Conference was called by President Roosevelt in 1909 to meet the needs of the orphaned, abandoned, and neglected children. It was the year in which the American Association for the Study and Prevention of Infant Mortality was organized. It was at a time when there was not a single fully developed pediatric clinic in the U.S.A.

As a result of this Conference the Children's Bureau was established in 1912, and it has continued to give at the Federal level leadership in the prevention of disease, improvement in the care of children and standardization of child labor practices. The American Association for the Study and Prevention of Infant Mortality was organized to solve a problem by what today is called the multidisciplinary approach. It focused the attention of the pediatrician, the public health nurse, social worker, statistician, public health officer, and interested lay groups on the problem of high infant mortality, with a resulting remarkable success. A reduction of the infant mortality rate from 150 to 40 has been accomplished in the last 40 years. We must not forget that in 1909 we did not know how many babies were born in the United States. Complete birth registration was not accomplished until 1933.

The Johns Hopkins Medical School was the first institution to inaugurate full-time professorships in medicine, surgery and pediatrics. In 1910 Dr. John Howland was appointed the first full-time professor in pediatrics at the Johns Hopkins Medical School. This was the first of the large number of outstanding pediatric clinics that now dot the country from east to west and north to south.

The second Conference under President Wilson set standards for maternity and child care and for child labor.

The 1930 White House Conference was called by President Hoover to study the present status of the health and well-being of the children of the U.S.A., to report what was being done, and to recommend what ought to be done, and how to do it. The pediatrician played an important role in this Conference. Fourteen volumes on Child Growth and Development, on Medical Care of Children and on Pediatric Education were the result of their efforts. The Conference focused the thinking of the pediatrician on the possibilities of group action, and no doubt had an influence in bringing about the organization of the Academy of Pediatrics and the American Board of Pediatrics. The report on pediatric education had far reaching results in increasing the hours devoted to the teaching of pediatrics in the medical schools as well as the inclusion of growth and development, and of the preventive aspects of pediatrics in undergraduate teaching.

The fourth White House Conference, called by President Franklin D. Roosevelt, was asked to consider "How a democracy can best serve its children and how can children be best helped to grow into the kind of citizens who will know how to preserve and protect our democracy." We sense here an appreciation of something more than just what can be done for the health, education and welfare of children. In spite of efforts to insure a well arranged follow-up program the general war efforts nullified many of its hoped for results.

The fifth, Midcentury, White House Conference on Children and Youth will hold its meeting December 3-7, 1950. The National Committee of the Conference was appointed by President Truman last August. It consists of 52 citizen leaders representing the professions, business, labor, agriculture, the laity, and for the first time, youth. Pediatrics is represented by Charles A. Janeway, Edward B. Shaw and Benjamin Spock. The other medical representatives in this Committee are Raymond B. Allen, T. Duckett Jones and William Menninger. In the past 10 years pediatricians have become increasingly more interested in the emotional growth and development of children. Gesell, Aldrich, Senn, Spock and many others have pioneered in this work.

It is, therefore, of particular interest to the pediatrician that "the Midcentury White House Conference on Children and Youth bases its concern for childen in the primacy of spiritual values, democratic practice and the dignity and worth of every individual. Accordingly, the purpose of this Conference shall be to consider how we can develop in children the mental, emotional, and spiritual qualities essential to individual happiness and to responsible citizenship, and what physical, economic and social conditions are deemed necessary to this development."

To accomplish these ends, the Conference shall:

(a) bring together in usable form pertinent knowledge related to the development of children and indicate areas in which further knowledge is needed;

(b) examine the environment in which children are growing up, with a view to determining its influence upon them;

(c) study the ways in which the home, the school, the church, the law, health and welfare agencies, other social institutions, individually and cooperatively, are serving the needs of children;

(d) formulate, through cooperative efforts of laymen and specialists, proposals for the improvement of parental, environmental, and institutional influences on children;

(e) suggest means whereby these proposals may be communicated to the people and put into action.

The actual meeting of the Conference will take place December 3 to 7 of this year. For the past two years work has been going on in many States preparing for the meeting. Last September the Executive Committee of the National Committee appointed four Advisory Councils, the first one on Participation of National Organizations, of which there are about 514 interested in children. This group, which includes representation from both the Academy and the American Pediatric Society, will keep their members informed and stimulate interest in the Conference purposes, report on programs related to the focus of the Conference, recommend topics for discussion of State or local units, and undertake special studies or projects.

The second Advisory Council is on State and Local Action and consists of the representatives of the various State Committees which, at the request of the President, were appointed by the governors in the 48 States. These State groups are working through regional and county committees to study their local conditions of child health, education, and welfare. The Academy reports on State Child Health Services have been of great service to these Committees. It is hoped that by the time of the December Conference most all of the 3076 counties will have accurate knowledge of the present status of their services for the child and a determination to improve them.

The third Advisory Council is that on Youth Participation. It is the first time that youth has participated in the various activities of a White House Conference. Ninety representatives of 40 youth serving organizations attended the first Advisory Council meeting. The success of their meeting augurs well for the contribution that youth will make

to the Midcentury Conference, and the nation-wide experience which it is gaining in this Conference, will enable youth to add to the success of future White House Conferences.

The fourth Advisory Council is one on Federal Governmental Participation. It draws its membership from 37 departments, bureaus, and agencies interested in the child. They have been most helpful in assigning personnel to the staff, conducting studies, gathering pertinent information on the health, education and welfare of the child and preparing a chart book showing trend data relating to the focus of the Conference.

So much for the information and materials that will be brought in from the various Advisory Councils to be studied, coordinated, and brought to the various informatory sessions and discussion groups of the December Conference.

In addition to the Advisory Councils, the Executive Committee has appointed Technical Committees on Fact Finding, on Communications, on Program, and on Finance.

The Fact Finding Committee with the group of fact finders of the staff, under the direction of Miss Helen Witmer, is collecting the known data on what constitutes a healthy personality as thought of in the theme of the Conference, and what role interpersonal relationships, constitution and environmental factors, various cultures, economic status play in its successful development. The group is studying the effect in healthy personality development of the present practices of such institutions as the family, schools, churches, health services, recreation, art activities, employment, the courts and social sciences, and making suggestions how these might be improved.

Thus the material flowing into the Conference from the Advisory Councils and the fact finding groups will form the basis on which recommendations will be made and National, State and local plans outlined for the next decade to come.

The Committee on Communications will serve two purposes; integrating the scientific material coming in from various sources and making it available to the public in such form that it may form the basis of a successful follow-up program. In addition, it will develop the usual publicity to interest the public in the Conference plans and objectives.

The Program Committees faces the difficult task of correlating the various pre-Conference findings of Advisory Councils and Committees in such a manner that after discussion, a well thought-out set of recommendations will result from the Conference, and give direction to work for children in the next decade. Out of this Conference should grow a great nation-wide movement for the betterment of conditions in which happy children will develop into responsible citizens.

The pediatrician is, naturally, interested in all of the health aspects of the development of a healthy personality. He has made an invaluable contribution to the Conference through the study of the American Academy of Pediatrics, the Children's Bureau and Public Health Service in all the 48 States. The following topics are illustrative of the type of health contributions that are being made to the 1950 Conference: "Constitutional and physiological factors relative to healthy personality development," "Developmental process in childhood and adolescence," "Program and methods for promoting positive mental health and their efficacy." Special reports are being prepared on obstetric aspects, school health, nutrition, dental health, pediatric education and the crippled child in relation to the theme of the Conference.

The pediatrician played an important role in the Conference of 1930 that resulted in great improvement of the physical health of children and he has just as important a role to play in this Conference to help to determine how we can develop healthy personalities in all our children.

H. F. HELMHOLZ, *M.D., Chief Consultant*
Washington, D.C.

NEWS AND ANNOUNCEMENTS

The University of Arkansas announces the acceptance of a gift of $500,000 from the William Buchanan Foundation of Texarkana, Ark., to the Department of Pediatrics of the School of Medicine principally to construct an additional 100 pediatric beds in the new University Hospital. This will be known as the William Buchanan Pavilion for Children. Construction will probably start before the end of 1950.

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The following members were elected officers by the American Pediatric Society at its Annual Meeting at French Lick Springs, Ind., on May 8-10, 1950: President, Dr. Bronson Crothers; Vice President, Dr. Stanley Gibson; Secretary-Treasurer, Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12; Recorder and Editor, Dr. Stewart Clifford.

The following individuals were elected to active membership:

Dr. Edith Boyd
Denver
Dr. Donald E. Cassels
Chicago
Dr. Sidney Gellis
Boston
Dr. Jerome S. Harris
Durham, N.C.
Dr. Allen J. Hill, Jr.
Minneapolis
Dr. Nelson K. Ordway
New Orleans
Alexander Schaffer
Baltimore
Dr. Robert L. Jackson
Iowa City
Dr. Jerome L. Kohn
New York
Dr. Wm. S. Langford
New York
Dr. Lyman T. Meiks
Indianapolis
Dr. Benjamin M. Spock
Rochester
Dr. Edward Pratt
Boston
Dr. Hale F. Shirley
San Francisco
Dr. Hulda E. Thelander
San Francisco

The following were elected to honorary membership: Dr. Robert Debre, Paris; Dr. Arvid Wallgren, Stockholm; Dr. Guido Fanconi, Zurich.

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The following members were elected officers by the Society for Pediatric Research at its Annual Meeting at French Lick Springs, Ind., on May 8-10, 1950: President, Dr. Harry H. Gordon; Vice-President, Dr. John M. Adams; Secretary-Treasurer, Dr. Robert Ward, 477 First Avenue, New York City 16.

The following are new members of the Society for Pediatric Research:

Forrest H. Adams, Minneapolis
Edward Ahrens, Jr., N.Y.C.
Fred H. Allen, Jr., Boston
James B. Arey, Philadelphia
James Bosma, Salt Lake City
William A. Brodsky, Cincinnati
James Etteldorf, Memphis
Clifford G. Grulee, Jr., New Orleans
Paul H. Hardy, Baltimore
Janet M. Hardy, Baltimore
Eugene Kaplan, Detroit
C. Henry Kempe, San Francisco
Saul Krugman, N.Y.C.
Charles Lowe, Minneapolis
Robert McKay, Burlington, Vt.
Julius B. Richmond, Chicago
Conrad M. Riley, N.Y.C.
Frederick Robbins, Boston
Frederic N. Silverman, Cincinnati
Selma E. Snyderman, N.Y.C.
Samuel Spector, Cleveland
Harry A. Waisman, Chicago
Clark D. West, Cincinnati

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Dr. Edwards A. Park, Baltimore, was awarded the George M. Kober medal by the Association of American Physicians at its annual meeting in Atlantic City, May 2-3, 1950. This is one of the highest honors in American medicine. Dr. Park is Professor Emeritus of Pediatrics at the Johns Hopkins Medical School. He has been President of the American Pediatric Society and a member of the Editorial Board of PEDIATRICS.

The Association of American Physicians at the same meeting conferred honors on 3 pediatricians by electing them to active membership in the Association. They are: Drs. Helen B. Taussig, Baltimore, Amos Christie, Professor of Pediatrics, Vanderbilt University, Nashville, and Paul Gyorgy, Philadelphia. Dr. Taussig is the first woman to be elected a member of the Association in its 63 year history.

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The American Board of Pediatrics, Inc., announces that oral examinations will be held at: Chicago—Oct. 13, 14 and 15, 1950; Boston—Dec. 1, 2 and 3, 1950.

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The following diplomates were certified by the American Board of Pediatrics, Inc.:

CINCINNATI—MAY 5, 6 AND 7, 1950

Allen, John Edward, 2316 Auburncrest Ave., Cincinnati
Armstrong-Seward, Catherine, Travis Clinic, S. Ragsdale St., Jacksonville, Texas
Barron, Samuel Harris, 1951 Irving Park Rd., Chicago
Becker, Arnold H., 124 Main St., Bristol, Conn.
Berrey, Bedford Hudson, 308 S. Third St., Harlingen, Texas
Beswick, Robert Cleon, 694 Lincoln Ave., Bellevue, Pittsburgh
Bills, Jack W., 117 Whittier, Idaho Falls, Idaho; presently at Children's Hospital, Cincinnati
Blanchard, Mercer C., 204 11th St., Columbus, Ga.
Bluestone, Seymour S., 525 Eastern Parkway, Brooklyn
Boles, Clifford Read, 769 Yale Ave., St. Louis
Brill, Thomas M., 1011 W. Masonic St., Gainesville, Fla.
Caro, Eugene Paul, 926 N. Wood Ave., Linden, N.J.
Collett, Robert Waterman, 1765 Sherman Ave., Denver
Coren, Sidney William, 1204 Colonial Ave., Norfolk, Va.
Davis, Jean Patricia, Salt Lake General Hospital, 2033 S. State St., Salt Lake City
DeLoache, William R., 20 Professional Bldg., Greenville, S.C.
Falkenstein, Leo, 556 W. 140 St., New York
Gibbs, Robert William, Loring Medical Bldg., 1409 Willow St., Minneapolis
Girdany, Bertram R., Babies Hospital, New York City
Grant, Henry Boone, 140 N. Franklin St., Rocky Mount, N.C.
Hoch, Peter Carl, 858 Metropolitan Bldg., Denver
Hoyt, Arthur W., Chickasha Hospital and Clinic, Chickasha, Okla.
Jones, Mason S., 406-12 Harries Bldg., Dayton, Ohio
Kay, Maurice Nathaniel, 183 Waterman St., Providence
Klein, Robert, Harriet Lane Home, Johns Hopkins, Baltimore
Klein, Seymour, 4753 Broadway, Chicago
Klingberg, William Gene, 500 S. Kingshighway, St. Louis
Lauderdale, James Abner, Jr., Rush Brothers Clinic, Meridian, Miss.
Lewis, Katherine Cecilia, La Rabida Jackson Park Sanitarium, Chicago
Lohrey, Ralph Conrad, 628 E. 185th St., Cleveland
Lueck, Wallace Wilson, 1009 Nicollet Ave., Minneapolis
Marienfeld, Carl J., 1819 W. Polk St., Chicago
McClure, David N., 7803 Clayton Rd., St. Louis
McGuire, William F., 401 N. Emporia, Wichita
McCrory, Wallace Willard, New York Hospital, Rm. 819, 525 E. 68th St., New York City
O'Brian, Etienne Raymond, 101 W. 7th St., Plainfield, N.J.
O'Toole, Roger L., 410 Lafayette Bldg., Waterloo, Iowa
Penn, Louis, 1505 Grand Concourse, Bronx
Robinson, Irving William, 835 W. State St., Trenton, N.J.
Scott, Oliver K., 437 E. 13th St., Casper, Wyo.
Semsch, Robert Daniel, 1409 Willow, Minneapolis
Shepard, Groom Shirley, 923 Ellis Ave., Lufkin, Texas
Silberbush, Flora Friedmann, 2076 E. 13th St., Brooklyn
Stein, Julius Daniel, 951 Park Ave., Bridgeport, Conn.
Stimson, Allan B., 68 Arnold, New Bedford, Mass.
Tilbury, Ross Claud, 544 E. Kingshighway, Shreveport
Treadway, James L., Jr., 710 Maison Blanche Bldg., New Orleans
Tudor, Robert Bruce, Quain Ramstad Clinic, Bismarck, N.D.
Wehl, Selma, 1536 51st St., Brooklyn
Weihl, Carl, 1008 Marion Ave., Cincinnati
Wolk, Arthur D., 69-39 Yellowstone Blvd., Forest Hills, N.Y.
Yeager, Otis Wayne, 2250 Highland Ave., Birmingham, Ala.

BOOK REVIEWS

BLOOD CLOTTING AND ALLIED PROBLEMS, edited by J. E. Flynn, New York, Josiah Macy, Jr., Foundation, 1949, $2.25, 231 pp.

The relatively new practice of bringing together for more or less informal conferences a small number of men who are acknowledged leaders in their respective fields for the purpose of discussion of problems in which they have a common interest is gaining increasing currency in many areas. The report of the transactions of the Second Conference on Blood Clotting and Allied Problems, held in New York on Jan. 24 and 25, 1949, indicates clearly how effective such conferences can be in catalyzing the exchange of information among persons with closely related problems to their mutual benefit, and how effective in clarifying issues and aims, resolving semantic difficulties, and bringing moot points into active debate.

The report records the discussion of 19 participants in the conference around 9 more or less formal presentations: Tocantins and Carroll, and Overman on thromboplastin inhibitor, Ferry on clot formation, Barker and Margulies on surface effects in clotting, Wright and Horan on zeta-potential studies, Flynn and Standley on the conversion of prothrombin to thrombin, Quick on platelets, and Sorenson and Wright on a synthetic anticoagulant. These papers take up 56 pages and set the stage for 107 pages of stimulating discussion, not including 27 pages of a special discussion of the problem of standardization of thromboplastin. There is a special section in addition on the preparation of lantern slides which many investigators will find useful in the presentation of data.

This book will be of most value to those physicians who have a special interest in blood clotting problems, none of whom should be without it. Others will find it informative and stimulating. Its usefulness might be increased if there were an index, but it can be readily appreciated that the effort involved in indexing such a volume might not be warranted by the potential gain in utility.

TRAINING FOR CHILDBIRTH, Herbert Thoms, M.D., New York, McGraw-Hill Book Company, Inc., 1950, $3.00, 114 pp.

This book presents the results and describes the obstetric program of prenatal training and the rooming-in plan as practiced at the Grace New Haven Hospital. If it accomplished nothing else, it would be timely in clarifying the many misconceptions of these 2 programs.

The training program is not planned with any idea that childbirth is painless but on the basis that it can be accomplished more easily if fear and the anxiety of facing the unknown are reduced. Prospective mothers, therefore, attend a series of 1 lecture and 2 exercise classes early in pregnancy and another series late in the 3rd trimester.

At the lectures the physiologic and mechanical aspects of pregnancy and labor are explained and questions answered. The classes are conducted by a nurse trained in physical therapy who teaches exercises aimed at increasing the tone of the muscle groups primarily involved in delivery and promoting physical relaxation generally during labor. No claim is made that this program results in painless childbirth. Analgesics and anesthetics are used as required.

Only 1 short chapter is devoted to the rooming-in plan which advocates 4-bed cubicle wards with an attached nursery in which the infant may be placed when the mother wishes to rest.

The results indicate that the program was highly successful in promoting relaxation and childbirth with a minimum of emotional tenseness. A significantly higher percentage of the mothers required no anesthesia and were fully conscious at the time of birth. There was uniform enthusiasm among the mothers toward the rooming-in part of the program.

CHILDBIRTH—YOUR QUESTIONS ANSWERED, Carl Henry Davis, M.D., and Donita Ferguson, Harper & Brothers, New York, 1949, $2.50, 183 pp.

This is a popular book written to provide information which is intended to allay anxiety for expectant mothers and fathers. The book does not achieve its purpose.

Much of the factual information presented is poorly chosen. For example, pregnancy in a patient

may be a severe risk. Nevertheless, the story of the 30 year old rheumatic patient who died 2 weeks postpartally, "but not before discovering a happiness her invalidism would otherwise have denied her" seems quite out of place. The entire discussion about rheumatic heart conditions and risk of pregnancy is presented in such a way that it can only stimulate intense fright and anxiety in the minds of both husbands and wives, where there has been a maternal history of rheumatic involvement.

The tone of writing at times is rather undignified and there is a general denial of the fact that, to most women, the period of pregnancy is a very unique and important experience.

There are many debatable pediatric statements presented as facts. The reviewer disagrees with the statement, "If you have a premature baby weighing less than five pounds, mother's milk is almost a necessity. . . . No baby formula is as good as mother's milk." The advice about the length of time necessary for adequate feeding at breast seems quite a good deal shorter than that observed by many pediatricians who have watched the nursing mother and infant.

The reviewer regrets that the format and simple language of the book is seriously invalidated by the poor selection of medical material. There is a somewhat belittling tone throughout as the fears and anxieties of the expectant mother are discussed.

HOSPITAL CARE IN THE UNITED STATES, Commission on Hospital Care, New York, The Commonwealth Fund, $4.50, 631 pp.

Many individuals and organizations have had a part in the making of this book. They have described influences and forces whose interaction has resulted in the present pattern of our hospital services, and documented their interpretations. The result is a source book of basic information which should be valuable for all students of hospital problems.

The Commission was appointed by the American Hospital Association, and chosen to represent a wide range of those providing hospital, health and welfare services, as well as the consuming public. Technical advisers were obtained, both from voluntary organizations and the United States Public Health Service. In an introductory statement, the Commission points out that we are far from having a "splendid system of hospitals." Diversity of background and objectives, among the sponsoring interests, has resulted in widely differing patterns of organization and control. Coordination of the activities of separate hospitals is rare. There are areas where hospitals are in uneconomic competition. There is uneven distribution, both of personnel and facilities.

Most of the book is devoted to painting things as they are, with a considerable amount of historical detail to give perspective. For example, 90 pages are devoted to tracing hospital evolution from the temple practice of ancient India and Greece to the complex institutions of the present, whose administration has become a profession in itself. Various attempts at solution of some of our present problems now being carried on under voluntary and governmental auspices are briefly described. One hundred eighty-one conclusions and recommendations are presented. The moral principles advocated are uniformly commendable, the methods recommended to achieve these ends, frequently vague.

This is a difficult book to read. Portions are prolix, and elsewhere the transition from specific instance to generality abrupt. As a source book, enriched by a good index and bibliography, it will prove valuable.